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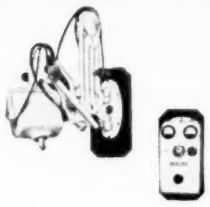

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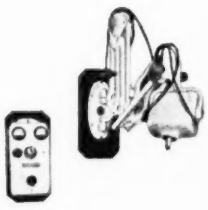

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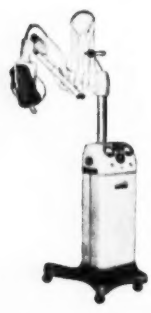

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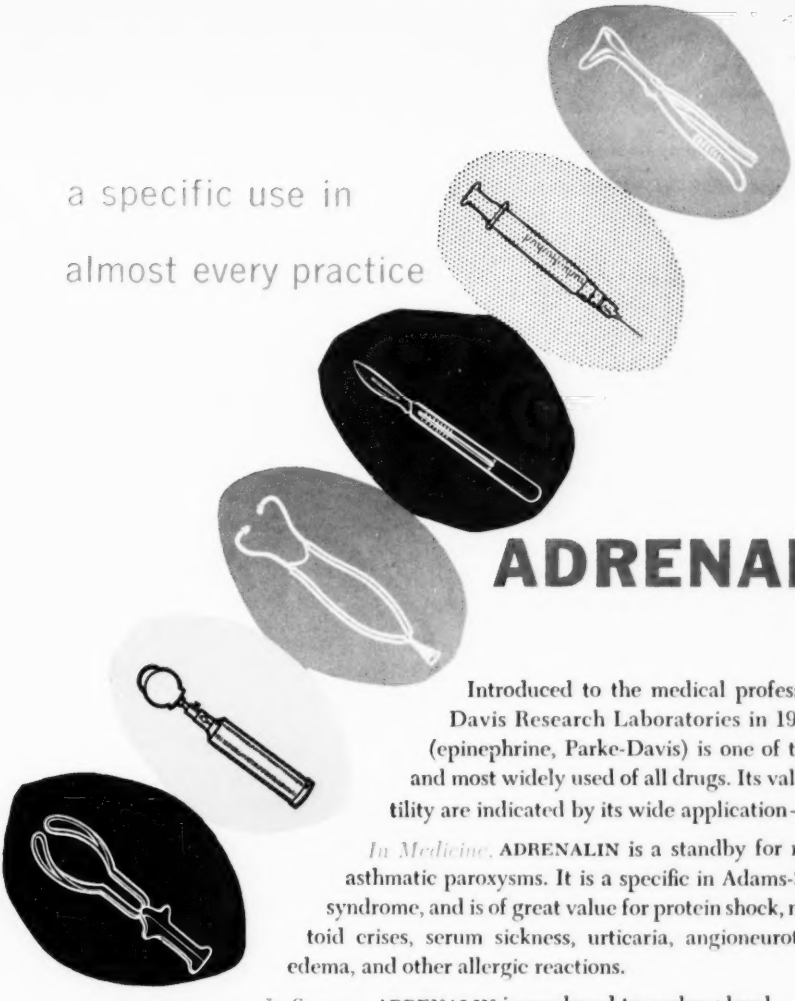

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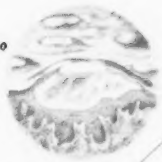
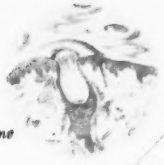
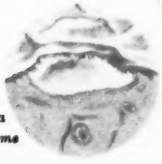

impetigo

skin infections and antibiotics


acne

pyoderma

folliculitis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1. *Bednar, G. A.: South. M. J. 46:298 (March) 1953.*
2. *Wright, C. S., et al.: A. M. A. Arch. Dermat. & Syph. 67:125 (Feb.) 1953.*
3. *Robinson, H. M., et al.: South. M. J. (in press).*
4. *Andrews, G. C., et al.: J. A. M. A. 146:1107 (July 21) 1951.*

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2. Stieglitz, E. J.: Geriatric Medicine, p. 848, 1943.

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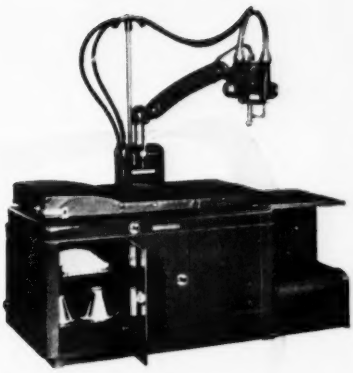

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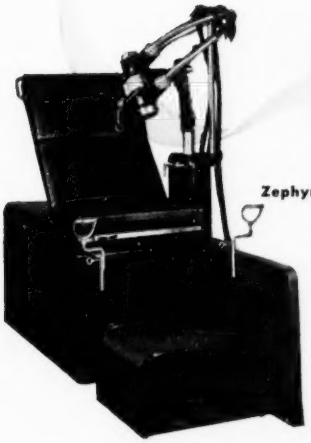

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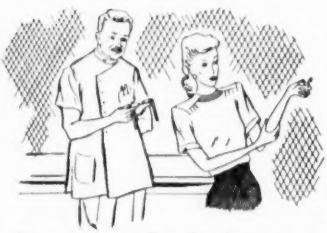

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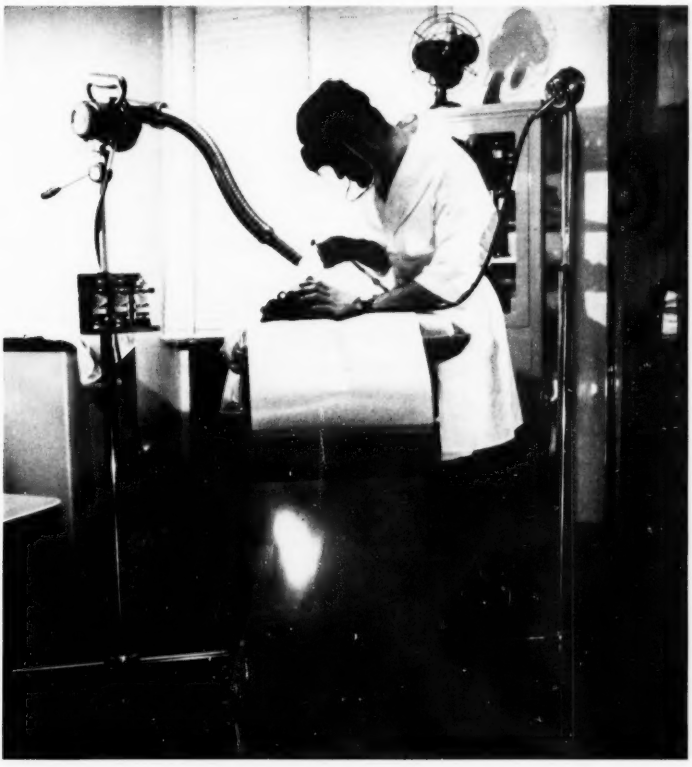

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SHERLOCK HOLMES AS A DERMATOLOGIST

With Remarks on the Life of Dr. Joseph Bell and the Sherlockian Method of Teaching

JOSEPH V. KLAUDER, M.D.
PHILADELPHIA

But if truth is stronger than fiction, then fantasy must sometimes attain astonishing heights of verisimilitude.—American Scientist **40**:380, 1952.

BEFORE discussing Sherlock Holmes as a dermatologist, and reporting the clinic he conducts and the Sherlockian method of teaching, it is pertinent to discuss his teacher, Dr. Joseph Bell (1837-1911).

Dr. Joseph Bell, who entered the medical school of the University of Edinburgh in 1821, later becoming professor of surgery, came from a distinguished family of physicians. His kinsmen were enrolled as members of the Royal College of Surgery, either a Benjamin or Joseph, for 140 years commencing in 1771.[1]

Bell was an excellent surgeon, a prolific writer, and popular as a teacher. His lectures and clinics in which he presented patients with a variety of diseases were always crowded. He would astound his students with his intuitive powers and keen observation, skill in eliciting facts and in deduction. He emphasized the importance of training the student's observant faculties. "Eyes and ears which can see and hear, memory to record at once . . . precise and intelligent recognition and appreciation of minor differences as the essential factor in all successful medical diagnosis."[2]

In his stress on the importance of observation he wrote: "I always impressed over and over again upon my students the vast importance of little distinctions, the endless significance of the trifles." "Nearly every handicraft writes its sign-manual on the hands. The scars of the miner differ from those of the quarryman. The carpenter's callosities are not those of the mason. . . . The soldier and sailor differ in gait. Accent helps you to district and, to an educated ear, almost to county. . . . With a woman, especially the observant doctor can often tell what part of her body she is going to talk about."[3]

Throughout his life he continued to amaze his circle through his keen observation and deduction. His daughter, Mrs. C. C. Stisted, recalls: "He would tell us where

From the Department of Dermatology, Graduate School of Medicine, University of Pennsylvania, Herman Beerman, M.D., Chairman.

Read at a meeting of (Sherlock Holmes Society) The Sons of The Copper Beeches of Philadelphia, Scion Society of the Baker Street Irregulars.

1. Obituary, Joseph Bell, Edinburgh M. J. **7**:454-463, 1911. Saxby, J. M. E.: Joseph Bell. An Appreciation by an Old Friend, Edinburgh and London, Oliphant, Anderson, and Ferrier, 1913.

2. Bell, Joseph: Mr. Sherlock Holmes, preface, in Doyle, A. C.: Study in Scarlet, New Ed., London, Ward, Lock & Bowden, 1894.

3. Wallace, I.: The Incredible Dr. Bell, Sat. Rev. Lit. **31**:7-8, 1948.

all the other passengers in the carriage were from, where they were going, and something of their occupation and habits. All this without having spoken to them. When he verified his observations, we thought him a magician." [3]

A. Conan Doyle (1859-1930) when a student at Edinburgh (1876-1881) was much impressed by the powers of observation and deductions of Joseph Bell, which inspired him to create Sherlock Holmes the prototype of Dr. Bell.[4] A. Conan Doyle writes [5]: "But the most notable of the characters whom I met was one Joseph Bell, surgeon at the Edinburgh Infirmary. Bell was a very remarkable man in body and mind. He was thin, wiry, dark,[6] with a high nosed acute face, penetrating grey eyes, angular shoulders, and a jerky way of walking. His voice was high and discordant. He was a very skilled surgeon, but his strong point was diagnosis, not only of disease, but of occupation and character. For some reason which I have never understood he singled out from the drove of students who frequented his wards and made me his out-patient clerk, which meant that I had to array his outpatients, make simple notes of their cases, and then show them in, one by one, to the large room in which Bell sat in state surrounded by his dressers and students.

"Then I had ample chance of studying his methods and of noticing that he often learned more of the patient by a few quick glances than I had done by my questions. Occasionally the results were very dramatic, though there were times when he blundered. Case No. 1 would step up.

"'I see,' said Mr. Bell, 'you're suffering from drink. You even carry a flask in the inside breast pocket of your coat.'

"Another case would come forward.

"'A cobbler, I see.' Then he would turn to the students and point out to them that the inside of the knee of the man's trousers was worn. That was where the man had rested the lapstone, a peculiarity only found in cobblers.

"In one of his best cases he said to a civilian patient, 'Well, my man, you've served in the army.' 'Aye, sir.' 'Not long discharged?' 'No, sir.' 'A Highland regiment?' "Aye, sir.' 'A non-commissioned officer?' 'Aye, sir.' 'Stationed at Barbados?' 'Aye, sir.' [7] 'You see, gentlemen,' he would explain, 'the man was a respectful man but did not remove his hat. They do not in the army, but he would have learned civilian ways had he long been discharged. He has an air of authority and he is obviously Scottish. As to Barbados, his complaint is elephantiasis, which is West Indian and not British.'

"All this impressed me very much. He was continually before me—his sharp, piercing eyes, eagle nose, and striking features. There he would sit in his chair with

4. A. Conan Doyle also mentioned Poe's Dupin as another source of Sherlock Holmes. Hespeth Pearson in "Conan Doyle—His Life and Art" suggests that Holmes' precise method first appeared in Voltaire's Zadig.

5. Doyle, A. Conan: Study in Scarlet, preface, New Ed., London, Ward, Lock & Bowden, 1894.

6. It is interesting to note that according to Douglas,[1] Bell's jet black hair went iron gray in three days of anguish during the final illness of his wife. Elsewhere, I recorded similar instances of this phenomenon (Psychogenic Aspects of Skin Diseases, J. Nerv. & Ment. Dis. **84**:249-273, 1936).

7. This was reproduced with modification in The Greek Interpreter, p. 504. The page number in this and subsequent similar references is to the Garden City Omnibus edition (The Complete Sherlock Holmes Garden City Books, Garden City, N. Y.).

fingers together—he was very dexterous with his hands—and just look at the man or woman before him. When I took my degree and went to Africa the remarkable individuality and discriminating tact of my old master made a deep and lasting impression on me, though I had not the faintest idea that it would one day lead me to forsake medicine for story writing."

Prior to Bell and contemporaneous with him there were other illustrious physicians who excelled in naming the patient's occupation at first glance. Tardieu,[8] in his comprehensive discussion of occupational stigmas, attributes this attribute to Corvisart (1755-1821), of the French School of Medicine, and his pupil Dupuytren (1777-1835), who, like Bell, was a renowned surgeon and diagnostician, and Trousseau (1801-1865), a French internist.

George Henry Fox,[9] in his "Reminiscences," discusses the keen observation of Hebra (1816-1880) and his vivid description of cutaneous diseases. "He rarely asked his patient any questions, but a hasty glance would usually enable him to tell more about the case than any one of his students would elicit by a lengthy catechism. . . . He would say, 'This man is a tailor,' and we soon found that he discovered this fact by feeling the needle pricks on the roughened forefinger. A hatter he recognized by some peculiar callus on the ball of the thumb. He could always guess the age and weight of a patient with unerring accuracy and tell us what province of Austria he came from." "While waiting for a patient to remove a bandage from his leg, Hebra casually glanced at him and remarked, 'This man is a Croat, 55 years of age, has pulmonary tuberculosis, and is a tailor by occupation.' . . . Wouldn't you know he was a tailor? Look at that little strip of drab cloth he has tied around the bandage. Tailors use that stuff for vest linings.'"

A. Conan Doyle's training under Dr. Bell is apparent in many of his Sherlock Holmes' stories. The following is a good example. In the "Adventures of the Norwood Builder," when a frantic young man burst into the room on Baker Street and announced himself as John McFarlane, Sherlock Holmes lazily replied, "You mention your name as if I should recognize it, but I assure you that, beyond the obvious facts that you are a bachelor, a solicitor, a Freemason, and an asthmatic, I know nothing whatever about you."

Campbell[10] reviews ample evidence in the Sherlock Holmes' stories to show that A. Conan Doyle had a "very good knowledge of medicine." "He was certainly an acute observer, and it is difficult to see why he was not an outstanding success in practice. . . ."

As an aid to A. Conan Doyle in his fascinating method of identifying the many varied characters that visited Baker Street, there were available in his era a number of medical references. These concerned marks of occupation, dysharmony of physique, deformities and other structural changes incident to occupation[11] (to wit the

8. Tardieu, A.: Mémoire sur les modifications physiques et chimiques que détermine dans certaines parties du corps l'exercice des diverses professions, pour servir à la recherche médico-légale de l'identité, Ann. hyg. **42**:388-423, 1894; **43**:131-144, 1850.

9. Fox, G. H.: Reminiscences, New York, Froben Press, Inc., 1926, p. 104.

10. Campbell, J.: Sherlock Holmes and Dr. Watson, A Medical Digression for Guy's Hospital Gazette Committee, London, Ash & Co., 1951.

11. In modern literature the volume of Ronchese, F.: Occupational Marks and Other Physical Signs: A Guide to Personal Identification, New York, Grune & Stratton, Inc., 1948, with its many illustrations and comprehensive review of literature is outstanding. The subject is likewise thoroughly discussed by Schwartz, L.; Tulipan, L., and Peck, S. M.: Occupational Diseases of the Skin, Ed. 2, Philadelphia, Lea & Febiger, 1947.

large right hand of Jabez Wilson indicating manual labor).[12] Tardieu [8] in 1850 (with extensive bibliography) reported on 48 different trades and occupations, and Vernois' [13] (1862) comprehensive study embraced 150 kinds of occupations. Campbell [10] reviews the several publications of Lane [14] (1886-1888) on anatomical changes induced by occupation.

It is doubtful, however, if Doyle needed to resort to the literature in consideration of his training under Bell, his creative mind and vivid imagination.

Figures 1 to 3 (a contribution to Sherlockiana) show marks of occupation and of profession (as discussed in their legends). With the exception of Figure 1 none of these marks are illustrated or discussed by Ronchese [11] or by Schwartz, Tulipan and Peck.[11] The callus shown in Figure 1 is labeled "handwriter's callus" by Ronchese in his text. He records its occurrence from a variety of implements employed in different occupations.

SHERLOCK HOLMES AND DERMATOLOGY

Keen observation, intense inspection of the subject, attention to details and apparent trifles so much emphasized by Sherlock Holmes are particularly pertinent to the dermatologist. It has been appropriately said that in diagnosis of contact dermatitis the dermatologist should be a good detective [17] with "the power of observation and that of deduction." [18] The diagnosis of cutaneous disease is essentially objective, and attention to morphologic and topographical detail (see Case 5) is important.

Indeed medical diagnosis in general is essentially deduction from premises elicited by inspection, examination, and the aid of instruments of precision and laboratory tests. The application of the laws of logic in diagnosis is pertinently discussed by Southard.[19] Diagnosis of cutaneous diseases should be the last to succumb to present trend in clinical medicine of diagnosis by short cuts afforded by a battery of laboratory tests and instrumental study.

It is disturbing when in demonstrating a patient with an eruption covered with scratch marks, a student naively asks the patient does the rash itch, to which Sherlock Holmes would reply, "the great unobservant—who could hardly tell a weaver by his tooth or a compositor by his left thumb.[20]

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12. The Red Headed League, p. 196.

13. Vernois, M.: De la main des ouvriers et des artisans au point de vue de l'hygiène et de la médecine légale, Ann. hyg. **17**:104-190, 1862.

14. Lane, W. A.: A Remarkable Example of the Manner in Which Pressure-Changes in the Skeleton May Reveal the Labour-History of the Individual, J. Anat. **21**:385-406, 1886-1887; The Anatomy and Physiology of the Shoemaker, ibid. **22**:593-628, 1887-1888; Some Changes in the Form of Acetabular Cavities, the Spinal Column, and Joints of the Hand, Illustrated by the Anatomy of the Charwoman, Guy's Hosp. Rep. **29**:359-367, 1887.

15. Footnote deleted.

16. Footnote deleted.

17. Sutton, R. L., Jr.: Contact Dermatitis: Practical Management and Identification of Cause Without Patch Testing, Arch. Dermat. & Syph. **59**:36-44, 1949.

18. The Sign of Four, p. 93.

19. Southard, E. E.: Diagnosis per Exclusionem in Ordine: General and Psychiatric Remarks, J. Lab. & Clin. Med. **4**:31-54, 1918.

20. Adventure of the Copper Beeches, p. 363.

Fig. 1.—Callus on the third finger of an accountant. Its site was at contact with a fountain pen held between the index and third finger.

Fig. 2.—A callus on the antihelix of a telephone operator. She used a unilateral ear receiver. A callus first appeared on the right ear, subsequently on the left ear after she changed the receiver to that ear. I have observed similar lesions on nuns from pressure of the starched white headpiece.

In presentday emphasis of psychosomatic relations in dermatology, the "sizing-up" of the patient, the demeanor, the quivering voice, the shivering eyelids, the recurring vasomotor flush, the solitary swallow, the emotional background, and environmental circumstances have considerable etiologic significance. This is illustrated in the case of a patient, a young girl who cowered before her mother. A glance sufficed in diagnosis of neurotic excoriations, and the remark of her mother sufficed in explanation, "No one can get a job with a face like that."

Fig. 3.—Callus-like involvement of the wrists of a baker. The affected skin was dry, thickened, and slightly scaly. With hands pointing upward, the flexor surfaces of the wrists were used to manipulate a thick layer of dough into a roll. The patient also had calluses on the dorsal surfaces of the last three fingers of the right hand. These fingers were used to pry loose a layer of dough from a table, causing friction of the dorsal surfaces against the table.

Psychiatrists have long had a (Sherlockian) code [21] of the nature and hue of clothing, of hair dress, and of ornamentation as an aid in psychiatric diagnosis. It is germane to this discussion to give this code.[22]

21. Flügel, J. C.: The Psychology of Clothes, London, Hogart Press, 1930.

22. Code of Clothes

Anal character: Love of orderliness—showing itself in exaggerated degree of cleanliness or neatness in manner of dress. Over-emphasis on possessions—buy new clothes but do not wear them, simply keeps them for future and derive great pleasure in hoarding them. Dislikes to throw out old clothing.

Obsessive compulsive men: Wear clean brown and white or black and white shoes.

Anxiety or anxiety hysteria: Loud colors, bright plaids, etc. Men wear loud, bright ties and shirts. Women often have immature hair styles.

Immature personality (female): "Little girl" hair styles (bangs, curls, shoulder-length hair in older women); not dressing "their age"—women over 30 trying to look in their teens or college age; bows or ribbons on hair; frills, bracelets; school rings and pins.

(Footnote continued on next page)

That this code was known to Sherlock Holmes becomes apparent in the case of Miss Morstan,[23] since her dress fitted the depressed female. "The dress was a sombre grayish beige, untrimmed and unbraided, and she wore a small turban of the

Fig. 4 (Case 1).—Symmetrical serous synovitis (Clutton's joints). The right knee was the first affected, the swelling appearing after injury when the child was roller skating and preceding interstitial keratitis. How Sherlock Holmes determined these circumstances without the aid of history is discussed in Case 1.

Immature personality (male): Older men in college clothes, "old school" ties; fraternity pins; argyle socks; loafers; moccasins, excessive use of sport clothes in a city dweller, etc.

Depressed (female): Excessive use of gray, pale or dark blue, drab browns and black. Women with dyed hair not caring enough about appearance to keep it dyed. Careless dress in a normally careful, fastidious woman.

Homosexual (female): Mannish hair style, copying male dress as nearly as possible, preference for rough, coarse materials.

Exhibitionist (female): Low necklines, dangling earrings, radical styles, ultramodern.

Homosexual (male): Aesthetic taste in clothes—fine materials, pastel shades—excess of yellow. Padded shoulders.

23. The Sign of Four, p. 97.

same dull hue, . . . her lip trembled, her hand quivered and she showed every sign of intense inward agitation." Her depressed state was well explained by "the strange mystery which overhung her life" and correlated her statement, "I have led a retired life."

REPORT OF CLINIC CONDUCTED BY SHERLOCK HOLMES

Mimicking his teacher, Dr. Joseph Bell, Sherlock Holmes stares at the patient while "his long white nervous fingers" [24] toy with his magnifying glass. He purposely knows nothing of their history and asks no questions. His method is to inculcate intensive inspection of the patient—the demeanor, the clothing, the skin and the eruption.

CASE 1.—Sherlock Holmes: This child as you can see is about 12 years of age. She is either the oldest or the only child of her parents. She injured her right knee roller skating, I would say about two months ago. Subsequently her eye became inflamed.

Mother: That is extraordinary. How do you know that? She is the oldest child and fell when roller skating ten weeks ago.

Sherlock Holmes: (addressing students). It is apparent that the child has a bilaterial swelling of the knees, the right is more swollen. It is nonpainful as is seen from her gait. She has photophobia and lachrymation of one eye. She is a girl between the ages of 8 and 15. These circumstances indicate Clutton's joints—nonpainful symmetrical serous synovitis [25] which invariably precedes interstitial keratitis. Like the latter,[26] the disease is at first unilateral and at times appears after injury, followed by involvement of the second knee. The first knee involved is invariably the more swollen one. The course of events requires weeks. Interstitial keratitis, in accordance with Kassowitz' law, most frequently affects the oldest child and in a large percentage of instances the only child. The symmetrical groove depressions on the sides of the fore part of the sole of her shoes suggests the wearing of roller skates.

CASE 2.—Sherlock Holmes: This patient is a retail fish dealer who cut his index finger when cleaning fish, I would say two weeks ago. Sensation of throbbing, burning pain disturbs his sleep and sense of stiffness of some finger joints impairs the use of his hand.

Patient: That is correct, sir, although I cut my finger 12 days ago the redness at its site has disappeared. It appeared on other uninjured fingers and spread onto the back of my hand (Fig. 5). The pain keeps me awake, my fingers feel stiff which interferes with work.

Sherlock Holmes: These circumstances and the distinctive purplish red color of the lesions make the diagnosis of Erysipeloid of Rosenbach [27] obvious.

24. The Sign of Four, p. 91.

25. Klauder, J. V., and Robertson, H. F.: Symmetrical Serous Synovitis (Clutton's Joints), J. A. M. A. **103**:236-240, 1934.

26. Klauder, J. V.: Ocular Syphilis: IV. Interstitial Keratitis and Trauma; Clinical, Experimental and Medicolegal Aspects, Arch. Ophth. **10**:302-328, 1933.

27. Klauder, J. V.: Erysipeloid as an Occupational Disease, J. A. M. A. **111**:1345-1348, 1938.

Student: How do you know the man is not an abattoir worker, a commercial fisherman, or was infected from handling dressed turkeys?

Sherlock Holmes: A commercial fisherman would not be as pale-faced as this patient. The retrogressing remains of the original laceration on the index finger is still apparent. "I have an abnormally acute set of senses,[28] and a faint but incisive scent of fish is apparent. This was confirmed when I noted, as you apparently did not, the few fish scales entangled in the patient's shoe laces," "Perhaps I have trained myself to see what others overlook" [29]—"great issues may hang from a boot lace." [30]

Case 3.—Patient: I did not come on account of my former skin trouble but I would . . .

Fig. 5 (Case 2).—Erysipeloid occurring after injury of a finger of a retail fish handler.

Sherlock Holmes: (interrupting the patient and addressing the students) I recall this patient several years back. I note he is still a waiter and has had trouble with his "jalopy." He is not employed in one of our deluxe restaurants. He comes to ask about his flat feet.

Patient: (in a surprised tone) Everything you said is correct.

Sherlock Holmes: The patient's black trousers with their satin band along their sides, his coat and vest of a different texture and color betray his occupation. He is enroute to his place of employment. The black stains around the cuticles of most

28. The Adventure of the Blanched Soldier, p. 1188, the olfactory sense of Sherlock Holmes detected the curious tarry odor emanating from the brown leather gloves worn by Ralph, the butler.

29. A Case of Identity, p. 214.

30. A Case of Identity, p. 219.

fingers, apparently of long duration, are not caused by his occupation as a waiter. I guessed he repairs his automobile. No deluxe restaurant would employ a waiter with such hands. Since he is a waiter he is entitled to have flat feet and this presumption is confirmed by the manner of his gait.

Case 4.—Mother: My little girl, age 3 years, has these scratched areas. The paroxyms of scratching are usually preceded by the statement, "Mother, I am going to scratch." Soon after its onset our Collie dog started to limp. I noticed, however, that when the dog is outside the house the limp disappears.

Sherlock Holmes: You need not tell me that your little girl is the oldest child and the scratching first appeared soon after the birth of your second child.

Mother: That is correct. How do you know that?

Sherlock Holmes: The itching will disappear if you divide your attention between your little girl and the baby. Similarly, resume patting the Collie. (Addressing the class) Much emphasis is now being given to psychosomatic relations in dermatology. The term is a new one—a new label for old wine. My teacher, Dr. Bell, demonstrated a number of instances. He was fond of quoting the American dermatologist, Dr. Hyde of Chicago, who wrote, "The widow must be made to lay aside the heavy crape-veil beneath which her urticaria plays."[31]

I would like to relate a remarkable example of psychosomatic expression that I have encountered.[32] "The person, who we will call Mrs. Seagrave, had been given a curious secondhand ring, snake-shaped, and dull gold. This she took from her finger at night. One night she slept with it on and had a fearsome dream in which she seemed to be pushing off some furious creature which fastened its teeth into her arm. On awakening the pain in the arm continued, and the next day the imprint of a double set of teeth appeared upon the arm, with one tooth of the lower jaw missing. The marks were in the shape of blue-black bruises which had not broken the skin. Mrs. Seagrave informed me that she did not know what made her think the ring had anything to do with the matter, but she took a dislike to the thing and did not wear it for some months, when being on a visit, she took to wearing it again. The same thing happened again, and the lady settled the matter forever by dropping her ring into the hottest corner of the kitchen range.

Case 5.—Sherlock Holmes: (addressing students) At our last meeting as a test of deductive reasoning, I suggested reading "The Adventure of the Golden Pince-Nez," and to explain, before reaching the end of the story, why, as I maintained, the assassin could not have possibly escaped by walking along the small strip of grass leading from the house to the road.[33]

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31. Hyde, J. N.: A Practical Treatise on Disease of the Skin, Ed. 4, Philadelphia, Lea & Febiger, 1897.

32. This is quoted from Doyle, A. C.: Memories and Adventures, London, Hadden & Stoughton, 1924, p. 114. It was told to Doyle by the person who experienced the phenomenon. He writes that he had no reason to doubt the veracity of her experience. Discussion of similar phenomena is afforded by Klauder, J. V.: Stigmatization, Arch. Dermat. & Syph. **37**:650-659, 1938.

33. Some former students of Dr. Udo Wile (Emeritus Professor of Dermatology, University of Michigan) informed me that in teaching dermatology he assigned reading of certain Sherlock Holmes' stories. Dr. Wile verified this (in a personal communication) and informed me that in teaching dermatology—class demonstrations, he employed the method of teaching herein described as the Sherlockian method.

It is to be recalled that in translation, the Sherlock Holmes' stories have been used as a textbook for the Egyptian police force, and the pre-Communist police force of China.

I wish to emphasize keen observation in diagnosis of an eruption. We need not ask any questions of the patient before us. This method . . . "sharpens the faculties of observation and teaches one where to look and what to look for."[34] The eruption began as a single lesion seen below the right clavicle. This initial lesion, invariably the largest one, is called the "primitive placque" or "herald patch." In this patient it was erroneously diagnosed as ringworm and painted with tincture of iodine. You will note faint trace of such treatment. As a result the lesion became secondarily eczematized, but that should not mislead you. From two or three to ten days, possibly a few weeks, following its onset a full-blown eruption appeared on the trunk. You will observe it is sparing on the neck, exempts the face, and abruptly stops about the midportion of the arms and thighs. Since the eruption is fully developed, its duration is about two weeks. The eruption does not itch, this does not explain the look of apprehension. The latter is probably caused by fear that he has contracted a venereal disease and to account for this anxiety I would conclude the patient is married.

(Sherlock Holmes passes his magnifying glass to a student and remarks) Closely examine several of the lesions with and without the glass and report everything you see.

Student: The color of the lesions is pink with a slightly reddish tint.

Sherlock Holmes: That is correct, it is usually designated as fawn-colored, chamois skinshade, or salmon pink.

Student: The lesions change in configuration on the sides of the neck and sides of the chest from round elsewhere to an oval outline. The lesions are rounded macules varying considerably in size and situated superficially. Their centers are clear but their borders are ringed with a fine, dry scale. These scales are triangular, their bases adherent to the border, their apices are loose and point toward the center of the lesion.

Sherlock Holmes: You have correctly described with one omission the disease called pityriasis rosea.[35] The omission is the wrinkled or crinkled surfaces of the lesions that are likened to crinkled cigarette paper. I hope that what I told you and the manner of telling it together with your minute description of the individual lesions will firmly fix in your mind the characteristic features of the disease.

Case 6.—The patient was obviously uncomfortable. His face and neck were red and swollen, his eyes almost closed. As the dressing, adherent to the scarlet oozing surfaces of the hands and forearms, was detached Sherlock Holmes looked him over in an abstracted fashion. "He sat silent for a few minutes with his fingertips pressed together and his gaze directed upward toward the ceiling."[36] He suddenly exclaimed.

This young man is an apprentice, he is left-handed, does considerable work reading blue prints or as a draftsman, in addition, experimental work with insulating

34. A Study in Scarlet, p. 13.

35. Klauder, J. V.: Pityriasis Rosea: A Clinical Study, Internat. Clin. **2**:78-84, 1923; Pityriasis Rosea with Particular Reference to Its Unusual Manifestations, J. A. M. A. **82**:178-183, 1924.

36. A Case of Identity, p. 219.

material including chloronaphthalenes and derivatives of cashew nut shell oil. The dermatitis has all the earmarks of a contactant cause. It represents an allergic reaction to cashew nut shell oil.

The patient: (in an astonished tone) How on earth do you know that?[37]

Sherlock Holmes: (addressing students) You will observe that his vest is worn across its lower portion from pressure against a table or drafting board. This source is confirmed by the tip of a drawing pen protruding from the vest pocket. He holds the pen in his left hand; that is evidenced by a callus on the side of the middle finger of the left hand (Fig. 1). A sparing number of lesions of chloracne on the sides of the neck points to recent exposure to chloronaphthalenes; otherwise they would be much greater in number. There are traces of varnish on some fingernails. Their thick, tenacious glazed appearance suggests two compounds—a varnish made from cashew nut shell oil, which like the chloronaphthalenes are used as insulating and moisture-resisting agents; the other, phenol formaldehyde resin. The latter is allergenic; in varnish form it is used as a glue by carpenters and cabinet makers, which he is not. Chloronaphthalenes are not allergenic whereas products of cashew nut shell oil are highly so causing most acute dermatitis of the exposed skin which the patient has.[38]

I have, as you know, studied marks of identification. "By a man's fingernails, by his coat-sleeve, by his boots, by his trouser-knees, by the callosities of his forefinger and thumb, by his expression, by his shirt-cuffs—by each of these things a man's calling is plainly revealed. That all united should fail to enlighten the competent inquirer in any case is almost inconceivable."[39] I conducted research on the distinction of antemortem and postmortem bruises[40] and have published studies[41] on "the influence of a trade upon the form of the hand, with lithotypes of the hands of slaters, sailors, corkcutters, compositors, weavers and diamond polishers."[42] "I have made a small study of tattoo marks and have even contributed to the literature of the subject."[43] . . . "There is no part of the body which varies so much as the human ear.[44] Each ear, as a rule, is quite distinctive and differs from other ones. In last year's Anthropological Journal you will find two short monographs from my pen on the subject."[45]

37. A Study in Scarlet, p. 6.

38. Klauder, J. V.: Actual Causes of Certain Occupational Dermatoses: A Study of 527 Cases, with Special Reference to Dermatoses Due to Mineral Oils, Arch. Dermat. & Syph. **48:** 579-600, 1943.

39. A Study in Scarlet, p. 13.

40. A Study in Scarlet, pp. 5 and 6.

41. For list of Sherlock Holmes' publications see: Roberts, S. C.: Dr. Watson, London, Faber & Faber, Ltd., 1931; Some Observations on Sherlock Holmes and Dr. Watson at Barts, St. Bartholomew's Journal, December, 1951. Catalogue, The Sherlock Holmes Exhibition presented by Adrian M. Conan Doyle, England, L. Middleditch Co., 1952. LaCour, T.: Ex Bibliotheca Holmesiana, Copenhagen, The Danish Baker Street Irregulars, 1951.

42. The Sign of Four, pp. 93 and 94.

43. The Red Headed League, p. 196.

44. Of the many structual abnormalities that have been attributed to congenital syphilis, apparently study of the ear has been neglected as a possible site of stigma of the disease. I (J. V. K.) therefore made photographs of the ears of children with congenital syphilis and compared them with similar photographs of nonsyphilitic children. Of the considerable variation in configuration of the ears of the two groups, no characteristic variation was apparent in the syphilitic group (unpublished study).

45. The Cardboard Box, p. 1053.

In a forthcoming publication I will discuss the value of Wood's fluorescent light in study of marks of violence on the cadaver and its use in examination of the hands, both antemortem and postmortem, as an aide in diagnosis of occupation. The fluorescent light is of aid in determining the duration of a scar and may be helpful in determining its source (Ronchese [11]).

CASE 7.—The patient presented four band-like areas of redness encircling both forearms (shown in Fig. 6). Sherlock Holmes made an awkward movement whereby he dropped his magnifying glass at the feet of the patient sitting in front of him. As he stopped to pick it up his face almost touched the affected right forearm of the patient.

(After dismissing the patient he addressed the students.) The patient has marital difficulties which doubtless explains recent separation from her husband. This is a logical deduction since she recently removed a ring from the fourth finger of the left hand, the conventional site of a wedding ring. Its removal is evidenced by remains of its indentation and slight congestion.

Fig. 6 (Case 7).—Bracelet-like lesions of dermatitis factitia and the "tell tale trickle tail" (an extension from the lesion on the left wrist) produced by Lysol. The patient admitted its use after examination by Sherlock Holmes. How he determined this is discussed in Case 7.

I again wish to emphasize keen observation and deduction in diagnosis of cutaneous diseases. As I have often said, "When you have eliminated all which is impossible, then whatever remains, however improbable, must be the truth." [46] In the case of this patient one can eliminate a spontaneous occurring cutaneous disease. No such disease in human beings [47] has such bizarre outline resembling the stripes of a zebra. Therefore the lesions must have been self-produced. In its production a liquid must have been used. This is apparent since its excess ran down the skin in droplet formation producing small pear-shaped areas of redness extending below the band-like lesions. I hope you observed these pear-shaped areas of redness which we could not discuss in the presence of the patient. They have been aptly called "the

46. The adventure of the Blanched Soldier, p. 1192.

47. Sherlock Holmes purposely specified "in human beings" since the eruption of "diamond back" disease in swine comprises many unique, bizarre designs suggestive of dermatitis factitia, see Klauder, J. V.: Erysipelothrix Rhusiopathiae Infection in Swine and in Human Beings: Comparative Study of Cutaneous Lesions, Arch. Dermat. & Syph. **50**:151-159, 1944.

tell tale trickle tail." The appearance of acute inflammation suggests that the irritant liquid was recently applied. In that event its odor should be present. To determine this I purposely dropped the magnifying glass and in picking it up I clearly detected a phenolic odor. In all probability Lysol was used.

The diagnosis of self-produced lesion—dermatitis factitia—frequently indicates hysteria and correlating the latter is the vivid hue of her attire. You should have observed that she wore a red hat, purple blouse, a checked skirt of yellow, red and green, and green shoes.

Student: (hesitatingly) Do you think, sir, that the self-produced band-like areas encircling the forearms are a displacement phenomenon to compensate for the removal of the wedding ring that encircles the finger?

Fig. 7.—Vitiligoid dermatosis in the postdermatic stage of pellagra in an alcoholic addict. Sherlock Holmes's discussion of this patient is embraced in Case 8.

Sherlock Holmes: Dermatologists have paid no attention to significance of lesions of dermatitis factitia. I would suggest that you refer to the writings of Freud. You will find ample discussion of configuration pertaining to the symbol of Priapus; in addition you may find discussion of configuration of self-produced cutaneous lesions since Freud attempts to explain the psychodynamics of many curious circumstances.

Second student: (naively) If dermatologists correlated personality types and skin diseases, psychiatrists character and type of clothing, can correlation be made between type of clothing and skin diseases?

Sherlock Holmes: It is likely that dermatologic psychosomaticists may come to such study.

CASE 8.—The patient presented a vitiligoid dermatosis (shown in Fig. 7).

Sherlock Holmes asked a student for the diagnosis.

Student: (proudly and mimicking his teacher) This man was given at place of work a new issue of rubber gloves. About three months after wearing them he and other fellow workers developed this depigmentation. It was erroneously diagnosed vitiligo. It represents what is called occupational leukoderma and is caused by monobenzyl ether of hydroquinone used as an antioxidant in the rubber.

Sherlock Holmes: (sarcastically) Your method of deduction is commendable but your range of observation is not. It did not extend beyond the patient's hands. "You see but you do not observe."—It is a capital mistake to theorize before one has data. Insensibly one begins to twist facts to suit theories, instead of theories to suit facts.[48] "Never trust to general impressions, but concentrate yourself on details."[49] Your premise that all gauntlet dermatoses are from wearing gloves is erroneous. You neglected to consider the classical gloved dermatitis of pellagra which the patient had. It is in the postdermatitic stage characterized by vitiligoid lesions presented by the patient.[50] In confirmation are the rounded pigmentary remains of a pellagrous dermatitis on the elbows, another region of predilection, the perlèche, the bronzing of the face, the dyssebacia, and above all the "corpus delicti" in diagnosis of pellagra—the faint but discernible pigmentary narrow band around the neck with an extension on the manubrium the remains of what is called Casál's (1681-1759) necklace. This is in tribute to a great Spanish physician who first observed and described pellagra in the early part of the 18th Century.

In all probability the cutaneous lesions appeared after prolonged alcoholic debauche. This is supported by his tottering gait, malnutrition, the dull, apathetic appearance, his desolate state and his tremors. During his debauche he drank an incredible amount of liquor and ate . . .

Patient: (interrupting—in a slurring speech). That is right, sir, for weeks I drank a quart or more of whiskey daily and ate only bean soup.

1934 Spruce St.

48. A Scandal in Bohemia, p. 179.

49. A Case of Identity, p. 220.

50. Klauder, J. V., and Winkelman, N. W.: Pellagra Among Chronic Alcoholic Addicts, J. A. M. A. **90**:364-371, 1928.

STREPTOMYCIN IN TREATMENT OF CUTANEOUS TUBERCULOSIS

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THE TREATMENT of cutaneous tuberculosis has undergone important progress during the last few years with the use of calciferol, streptomycin, *p*-aminosalicylic acid, thiosemicarbazone, and isoniazid.

In this paper I shall first give a short review of some different forms of cutaneous tuberculosis treated with streptomycin, and then emphasize my point of view on the value of this antibiotic and indications for its use in these conditions.

CLINICAL RESULTS

Among the localized types of cutaneous tuberculosis, scrofuloderma was treated with streptomycin. In the majority of these cases the results were most satisfactory. In cases with ulceration, in a short time the drainage of the fistulae stopped entirely, and the ulcerations healed gradually. In some cases the antibiotic was given parenterally as well as locally by instillation into the fistulous tracts or, in cases without ulceration, by intranodular injection. Injection of streptomycin into the tuberculous nodes once every three days resulted in the shrinking of the nodes and their disappearance in a few weeks. When it is used locally, a high concentration of streptomycin is brought directly into the lesions.

I obtained good results also in the treatment of tuberculosis verrucosa with streptomycin. In these cases, crusts and pus as well as the warty growths disappeared gradually, and a concentric cicatrization of the lesions was obtained in a rather short time.

In cases of lupus vulgaris—except the tumidus, ulcerative, vorax, and evolutional types—streptomycin did not give results comparable to those obtained with calciferol. In nonulcerative lupus vulgaris calciferol is undoubtedly the best remedy available at this writing.

Combined Treatment.—In persistent cases of localized cutaneous tuberculosis of different forms I used, with appreciable results, combinations of streptomycin with *p*-aminosalicylic acid (by mouth and locally) and streptomycin with calciferol.

I may safely say that these combined treatments play an additive or synergistic role.

Among the tuberculids, the papulonecrotic tuberculid, although sometimes responding to the streptomycin treatment, did not in most cases clear up with this treatment. Even in some cases in which the first results were satisfactory recurrences occurred after a short time. In one of those cases successive crops occurred within one month and in another within two and a half months after the apparent healing.

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I obtained no positive results in any cases of sarcoid treated with streptomycin. This treatment did not cause any change in the nodes, and I even witnessed the appearance of many new nodes during the period of treatment.

The same thing may be said for the fixed forms of lupus erythematosus which were also treated with streptomycin.

COMMENT

The number of patients treated with streptomycin was 31, divided as follows:

Tuberculosis colliquativa (scrofuloderma)	9
Lupus vulgaris	10
(*a*) Ulcerated	4
(*b*) Nonulcerated (planus 3; tumidus 3)	6
Tuberculosis verrucosa	4
Papulonecrotic tuberculid	2
Lupus erythematosus, fixed form (chronic discoid)	3
Sarcoids	3
(*a*) Darier-Roussy type	2
(*b*) Erythema induratum	1

Although a few of the patients had visceral or bone tuberculosis, most of them were free from active systemic tuberculosis. The total dose of the antibiotic used was 25 to 82 gm. It was given usually as 1 gm. a day. The injections were of 0.50 gm. each, repeated every 12 hours. In some of the cases the antibiotic was also used locally. The best results were obtained in tuberculosis colliquativa and verrucosa, and in ulcerative and tumidus lupus vulgaris. However, we did not obtain any results in the cases of lupus vulgaris planus, sarcoids, lupus erythematosus, and papulonecrotic tuberculid.

In the persistent cases, combined treatments gave very good results.

Two points were achieved with the use of combined treatments. First, the patients were under the influence of two medicines, and second, resistance to streptomycin was thus checked.

As the dosage of the antibiotic was well balanced, no intolerance was observed among the patients, and the treatments were not stopped in any of them because of toxic reactions.

Some of the patients who showed bad general health before treatment were much better afterward, and the sedimentation rate which was increased before streptomycin treatment returned to normal in most cases.

In those cases in which treatment was satisfactory, appropriate tests made at frequent intervals showed no signs of recurrence.

SUMMARY AND CONCLUSIONS

From what has been reported, the following clinical conclusions may be drawn:

Streptomycin therapy gives best results in the lesions in which the Mycobacterium tuberculosis can be traced or those which give positive bacilliary findings after guinea-pig inoculations. The fresher the lesion and the richer it is in bacilli, the better the response to streptomycin. Thus in fresh cutaneous lesions results are better than in the chronic, organized, fibrous forms.

Considering the very good results obtained in the treatment of some forms of cutaneous tuberculosis with streptomycin, I may say that Charpy's method has lost some of its indications. Except in the ulcerated and tumidus forms, calciferol treat-

ment still holds first place in the treatment of lupus vulgaris. However, in some cases in which the disease does not yield to vitamin therapy or in which calciferol is contraindicated streptomycin is the drug of next choice.

Among the best indications for streptomycin therapy are ulcerative and tumidus lupus vulgaris, scrofuloderma, and tuberculosis verrucosa. In persistent cases, combined treatment with *p*-aminosalicylic acid or calciferol may be used with good results.

Streptomycin is ineffective in the treatment of tuberculids. As thiosemicarbazone and isoniazid have not been extensively used in the systemic treatment of cutaneous tuberculosis, I shall not be able to give a clear view on this subject. I have used both these drugs in a few cases of localized cutaneous tuberculosis, and although I obtained promising results, I think that streptomycin used alone or in combination with *p*-aminosalicylic acid or calciferol is a very active agent and its advent in the dermatological field has obviously bettered the prognosis of some forms of cutaneous tuberculosis.

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CARBUNCLE CAUSED BY GAFFKYA TETRAGENA TREATED WITH OXYTETRACYCLINE (TERRAMYCIN)

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A CARBUNCLE [1] is a necrotizing infection of the skin and subcutaneous tissue that is usually due to the hemolytic Staphylococcus aureus. If untreated, this lesion may result in prolonged morbidity, a long healing period, some metastatic infections, and an appreciable mortality. Many methods of treatment have been advanced, including use of external heat, ointments, x-ray therapy, surgical intervention, and antibacterial agents used systemically and locally.

The following is a case report of a patient in whom a carbuncle developed from which only Gaffkya tetragena was cultured and which receded completely with peroral oxytetracycline (Terramycin) therapy.

REPORT OF A CASE

F. L., 35-year-old white male bartender, was admitted Aug. 15, 1952, to the dermatologic service because of a dermatitis of the legs of three months' duration. In 1943, portions of both tibia had apparently been removed to repair an injury to the right wrist. He had been admitted to this hospital on three previous occasions because of chronic alcoholism, alcoholic gastritis, and peripheral neuritis.

Three months prior to admission, he had noted a pruritic and painful ulcerated eruption in the areas of the surgical scars on the anterior surface of the legs. The dermatitis had become worse with self-medication, and upon admission he had an ulcerated exudative scaly hyperpigmented and purpuric dermatitis on the anterior surface of the distal halves of the legs. The rest of the physical examination gave results which were essentially negative, as were all the results of laboratory findings, except that the liver-function tests showed some abnormality. The cephalin cholesterol flocculation was 1+; the van den Bergh test was positive, 0.45 mg. per 100 cc. direct and 1.6 mg. indirect; the sulfobromophthalein (Bromsulphalein) sodium test showed 11.5% retention after 10 minutes; the prothrombin time was 13.4 seconds (control was 15.6 seconds), and the total protein was 7.2 gm. per 100 cc., with 3.8 gm. albumin and 3.4 gm. globulin (albumin-globulin ratio, 1.1/1.0).

Treatment consisted of bed rest, use of multivitamins, barbiturates, aluminum acetate solution compresses (1 to 32), chlortetracycline (aureomycin) ointment, and penicillin, 300,000 units intramuscularly twice daily for 22 days. Twenty days after admission there were only residual hyperpigmentation and a small remaining ulcer on the left leg. He was being considered for discharge when, on Sept. 8, a small carbuncle was noted over the angle of the left mandible; this was associated with fever and chills. Parenteral penicillin, 300,000 units twice daily, was

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1. Dale, W. A., and Haug, C. A.: Treatment of Carbuncles with Local Penicillin Injections, J. A. M. A. **149**:527-530, 1952.

prescribed Sept. 9, but within 48 hours generalized urticaria had developed. On Sept. 11 the penicillin administration was discontinued, a culture of the purulent material in the carbuncle was made, and peroral oxytetracycline, 250 mg. four times daily, was prescribed. By this time, the carbuncle had continued to extend in size, and the area of induration was now about 8.0 cm. in diameter, with a peripheral zone of erythema involving the left cheek and the left anterior cervical area. The anterior cervical lymph nodes were markedly enlarged and tender, and intermittent hyperpyrexia, chills, and sweats continued.

Within two days of oxytetracycline therapy the lesion became localized and fluctuant, and the systemic manifestations subsided. In eight days the indurated portion of the carbuncle was reduced to 3.5 cm. in diameter; in the center there was a 2.0 cm.-sized fluctuant area with considerable purulent exudation. The carbuncle was completely healed on the 15th day of the oxytetracycline treatment, and he was discharged well Oct. 3. Repeat bacteriologic cultures were performed one day and again seven days after initiation of the oxytetracycline therapy.

The original culture taken Sept. 11, as well as another taken on Sept. 12, revealed pure cultures of G. tetragena.[2] The culture taken Sept. 18 after seven days of oxytetracycline treatment yielded no growth. The organism grown in pure form was identified both times by the characteristic growth at 37 C in thioglycolate broth (BBL No. 140). The colonies were heavily seeded in the oxygen-poor portion of the tube, and the morphology consisted of uniform-appearing tiny tails; growth was good at 24 hours. Gram stains of the growth in the broth showed tetrads of tiny Gram-positive cocci. No growth occurred at 37 C on blood agar base (BBL No. 168) containing 5% defibrinated rabbit blood under aerobic and high carbon dioxide tension (candle-jar) and on anaerobic blood agar base (BBL No. 139) containing 5% defibrinated rabbit blood.

COMMENT

Since the discovery of Micrococcus tetragenus (now called Gaffkya tetragena) by Gaffky in 1881,[3] not over 200 recorded cases of infection have been attributed to this micro-organism. It was recognized as a nonpathogenic organism frequently encountered on the face and neck and in tuberculous cavities until 1886, when Jakowski [4] found it to be a pathogen. Reimann [5] stated, in 1935, that it was a not uncommon cause of disease but that it was often disregarded or unrecognized in this country. He found more than 170 cases of G. tetragena infection reported from other countries and only two in the American literature. Since then, at least seven other cases of infection caused by this organism have been reported in this country. The organism [5] is of comparatively low virulence and becomes invasive only when the resistance of the host has been reduced. When infection occurs, it resembles the local suppuration and septicemia due to the closely related Staphylococcus. G. tetragena has been reported to have been the etiologic agent in septicemia, arthritis, meningitis, endocarditis, pneumonia, prostatitis, empyema, and glomerulonephritis. Reimann [5] reported a nonfatal case of infection with septicemia, arthritis, and meningitis. He [6] described in great detail the variant

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forms of the cultures and microscopic features. Since then, in the American literature, there have been case reports,[7] of septicemia, meningitis, pneumonia, penile ulcer, ulcerative stomatitis, and endocarditis.

The effect of antibacterial therapy has varied from case to case. Sulfonamides were not beneficial in recent cases by Tobin [7b] and by Leach and Medinger,[7c] but were helpful in the case reported by Criscitiello.[7e] Penicillin was given in large doses by Boynton [7g] in a case of subacute bacterial endocarditis, without benefit; even in vitro the G. tetragena was noted to grow very freely in the presence of penicillin and streptomycin. Recently, Cuya [8] reported excellent results when he used oxytetracycline irrigations of purulent maxillary sinusitis when G. tetragena was the etiologic agent.

Our report concerns another example of a suppurative infection caused by this organism. In the patient, a chronic alcoholic, a severe carbuncle developed while he was being hospitalized for a dermatitis of the leg. During two days of penicillin therapy, the carbuncle became larger and more inflamed, and the systemic symptoms of fever and chills continued. With oxytetracycline therapy, the carbuncle localized, underwent involution, and the systemic symptoms abated. G. tetragena was obtained in pure culture on the day oxytetracycline therapy was begun and on the following day. Seven days after the initiation of this treatment, the abscess was sterile.

SUMMARY

A case is reported of a severe carbuncle caused by G. tetragena with prompt response to oxytetracycline (Terramycin) therapy.

The literature concerning G. tetragena infections is briefly reviewed.

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OBSERVATIONS ON PERIPHERAL CIRCULATION IN PSORIASIS

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PREVIOUS work[1] has demonstrated that patients with lupus erythematosus have an altered peripheral circulation, as demonstrated by changes in the form of the photoelectric plethysmogram of the fingers. It is the purpose of this paper to present evidence that the same kind of changes exist in the peripheral circulation of patients with psoriasis. This alteration in the peripheral circulation is similar to that reported in arteriosclerosis,[2] hypertension,[2] pseudoxanthoma elasticum,[3] and scleroderma.[4]

MATERIAL AND METHODS

Studies were made on 28 normal subjects and on 11 patients with psoriasis. The extent, acuity, or activity of the psoriasis was not recorded except to note that there was no clinical evidence of nail involvement at the time of the studies. Also, none of the patients had clinical or radiological evidence of hypertension or arteriosclerosis.

The photoelectric plethysmograph used in this study was a modification of that described by Hertzman.[5] A beam of light was directed through the terminal phalanx and fell on the sensitive element of a photoelectric cell. Variations in the intensity of light transmitted through the finger due to changes in the blood content which occurred with each heart beat were detected by the photoelectric cell and recorded by means of a capacity-coupled amplifier and a Cambridge electrocardiograph.

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The shape of the plethysmogram may be recorded by measuring certain components of the wave. In this study we measured the crest time and the pulse cycle time. The crest time is the time from the beginning of the anacrotic limb to the peak of the wave, and the pulse cycle time is the interval between the beginning of successive anacrotic limbs. Since the crest time is a function of the pulse rate, Dillon and

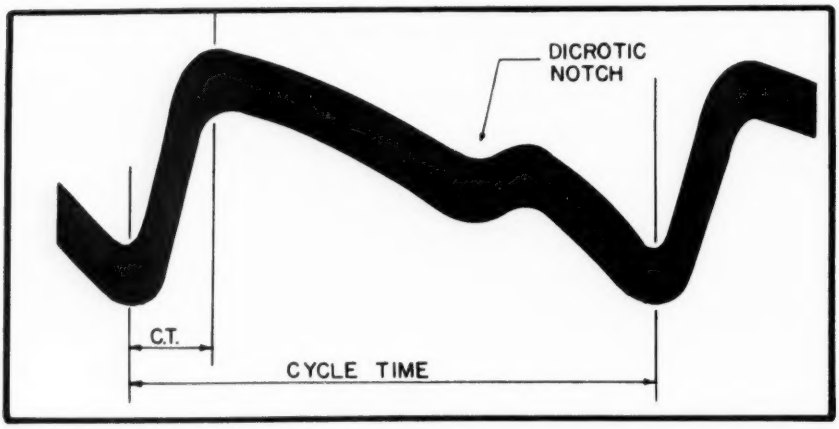

Fig. 1.—Enlargement of photoelectric plethysmogram obtained from middle finger of normal subject. Measurements referred to in text are crest time (C. T.) and cycle time.

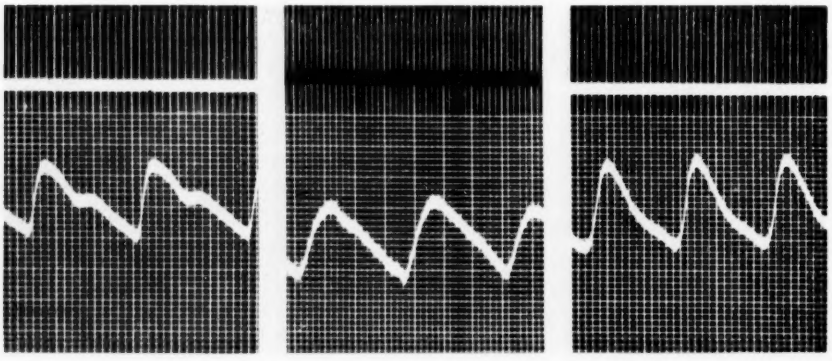

Fig. 2.—Photoelectric plethysmograms of middle finger pad illustrating wave form in normal (left) and in two patients with psoriasis (middle and right). Note prolonged crest times and obliterated dicrotic notches in patients with psoriasis.

Hertzman [2] have expressed the crest time in per cent of the cycle time and have found that this value is normally between 10 and 20%. A sketch of the normal finger plethysmogram is shown in Figure 1.

RESULTS

The normal photoelectric plethysmogram is composed of a steep anacrotic limb which comes to a rather sharp peak and a catacrotic limb with a sharply defined dicrotic notch. The plethysmogram of a patient with psoriasis has a different

appearance. The slope of the anacrotic limb is not as steep, with a resultant increased crest time, and the dicrotic notch on the catacrotic limb is poorly defined or obliterated.

Examples of photoelectric plethysmograms of a normal subject and of two patients with psoriasis are presented in Figure 2. The values of the crest times in per cent of the cycle times are presented in the table.

Statistical analysis reveals that this difference in values could occur by chance on less than one occasion in one thousand and indicates that patients with psoriasis as a group have abnormal photoelectric plethysmograms. Although crest times were within normal values in five of the patients, the dicrotic notch was absent in one of these (L. M.)

COMMENT

The results of this work indicate that there is a vascular dysfunction in areas which are remote from the sites of visible lesions. Previous experimental studies of patients with psoriasis have suggested an abnormality of the general peripheral

Values of Crest Times in Percentage of Cycle Times

	Crest Time in % of Cycle Time
Mean and standard deviation of 28 normals	15.31 ± 3.004
Patients with Psoriasis	
H. C.	15.0
G. K.	15.6
L. M.	15.8
A. M.	16.7
J. S.	17.9
J. C.	20.0
M. H.	22.2
E. C.	22.8
L. B.	25.0
O. L.	26.3
H. M.	27.8
Mean and standard deviation	20.46 ± 4.617

* T value of 4.11.

vascular system. Thus Madden [6] found capillary dilatation and perivascular leucocytic infiltration on histologic examination of clinically uninvolved skin. Milberg [7] has recently reported an abnormal course of the reactive hyperemia following vascular occlusion in the uninvolved skin of patients with psoriasis. Finally, the studies of Herrmann and Kanof [8] on the fluorescein pattern of dermatoses also suggest that the psoriatic process may affect the minute blood vessels of the skin.

It has been pointed out elsewhere [9] that abnormalities in photoelectric plethysmograms of the type reported here may arise from either functional or organic defects

6. Madden, J.: Histologic Studies of Uninvolved Skin of Patients with Psoriasis, Arch. Dermat. & Syph. **44**:655-664 (Oct.) 1941.

7. Milberg, I. L.: The Reactive Hyperemia Response of the Uninvolved Skin of Patients with Psoriasis, J. Invest. Dermat. **9**:31-39 (July) 1947.

8. Herrmann, F., and Kanof, N. B.: The Fluorescein Pattern of Dermatoses, J. Invest. Dermat. **8**:421-432 (June) 1947.

9. Hertzman, A. B., and Roth, L. W.: The Reactions of the Digital Artery, and Minute Pad Arteries to Local Cold, Am. J. Physiol. **136**:680-691 (June) 1942.

of the circulation. Furthermore, the presence of circulatory abnormalities in the presence of fully developed disease does not provide information on the mechanism or origin of a disease process, since such changes could either precede or follow the development of the disease. The evidence presented here does offer support to and is consistent with the concept that psoriasis has widespread effects throughout the body.

SUMMARY

Photoelectric plethysmograms of the fingers of 28 normal controls and of 11 patients with psoriasis have been studied.

The plethysmograms of patients with psoriasis as a group are abnormal. The crest times are prolonged, and the dicrotic notches are obliterated.

This study furnishes additional evidence of a vascular dysfunction in patients with psoriasis.

CORRECTIVE SURGICAL PLANING OF SKIN

New Technique for Treatment of Acne Scars and Other Skin Defects

ABNER KURTIN, M.D.
NEW YORK

IT HAS been reported that sandpaper abrasion of the skin is an effective method for the correction of acne scars [1] and tattoo marks.[2] As a routine treatment, however, it was considered that this procedure had certain inherent drawbacks.

In the first place, administration of a general anesthetic, with the known risk involved, may not be advisable in a reconstructive operation. The inhalation apparatus interferes on the facial area, which, of course, is the commonest operative site.

Secondly, sandpaper presents a relatively broad surface which makes it difficult to treat irregular contours and does not permit differential abrasion of adjacent areas. The possibility of silica granulomas caused by small buried particles must be considered as a calculated risk.

Despite these disadvantages, the clinical benefit in the reported cases was such as to warrant further experiment with the abrasion technique. After five years of trial, a successful modification has been developed which eliminates many of the above disadvantages. This modification provides a simple office procedure done under local anesthesia which employs a safe abrading device and which permits delicate control in a bloodless field.

The following is a report on 273 cases, some followed for as long as four years, in which the above goals were approached.

PROCEDURE

Anesthesia.—Ethyl chloride refrigeration seemed to offer a number of advantages. It can be rapidly applied to a specific area. The frozen skin is not only insensitive, but bloodless and rigid as well. The rigidity permits adequate resistance to the abrading instrument, so that elevations and depressions maintain their relative positions under pressure. When used on the face, a very small amount of ethyl chloride, if inhaled, offers the gratuitous advantage of further relaxation of the patient.

One disadvantage of the use of ethyl chloride is the initial burning sensation which is felt for a few seconds before freezing occurs. Another disadvantage of this agent is the possibility of cold devitalization of tissue.

After balancing advantages against disadvantages of this material, experimentation was begun. It was found that pain could be minimized by prechilling the area to be treated with ordinary ice packs applied to the skin. Clinical observation has established that healing is not interfered with by this process, presumably because most, if not all, of the frozen skin is removed during the operation.

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1. McEvitt, W. G.: Treatment of Acne Pits by Abrasion with Sandpaper, J. A. M. A. **142**:647-648 (March 4) 1950.

2. Iverson, P. C.: Surgical Removal of Traumatic Tattoos of the Face, Plast. & Reconstruct. Surg. **2**:427-432 (Sept.) 1947.

In the light of the above considerations, the following procedure has proved effective.

Male patients are instructed to shave closely before the operation. The skin is cleansed by careful washing with ordinary soap. All cosmetics are removed. A special plastic ice pack has been devised which covers the entire face.[3] This pack contains propylene glycol (5%) in water. This chemical permits adequate chilling without hardening in the freezer compartment of the refrigerator. The pack is administered for 20 minutes. The face is then cleansed with alcohol.

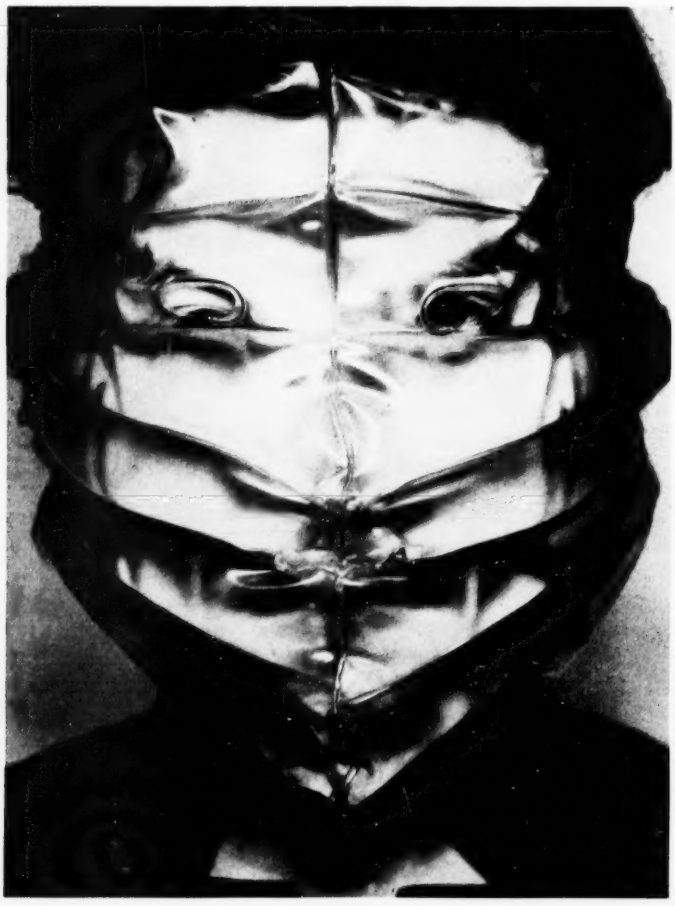

Fig. 1.—Face-fitted cold pack.

Ear and nose orifices are plugged with cotton to prevent inadvertent spraying of these areas. The eyes are protected with gauze held firmly in position by the assistant.

A current of air is directed on the area to be treated to accelerate evaporation and consequent freezing. Originally, a small hand blower was used successfully. This was held and directed by the assistant. Subsequently, a mounted blower was developed which permitted direction of the stream by the operator and which also freed the assistant's hand.[3]

The ethyl chloride is sprayed from a standard glass container in a coarse stream. Freezing occurs in a few seconds. The depth of freezing can only be determined by experience. Moderate

3. Manufactured by Robbins Instruments Company, 520 Fifth Ave., New York 36.

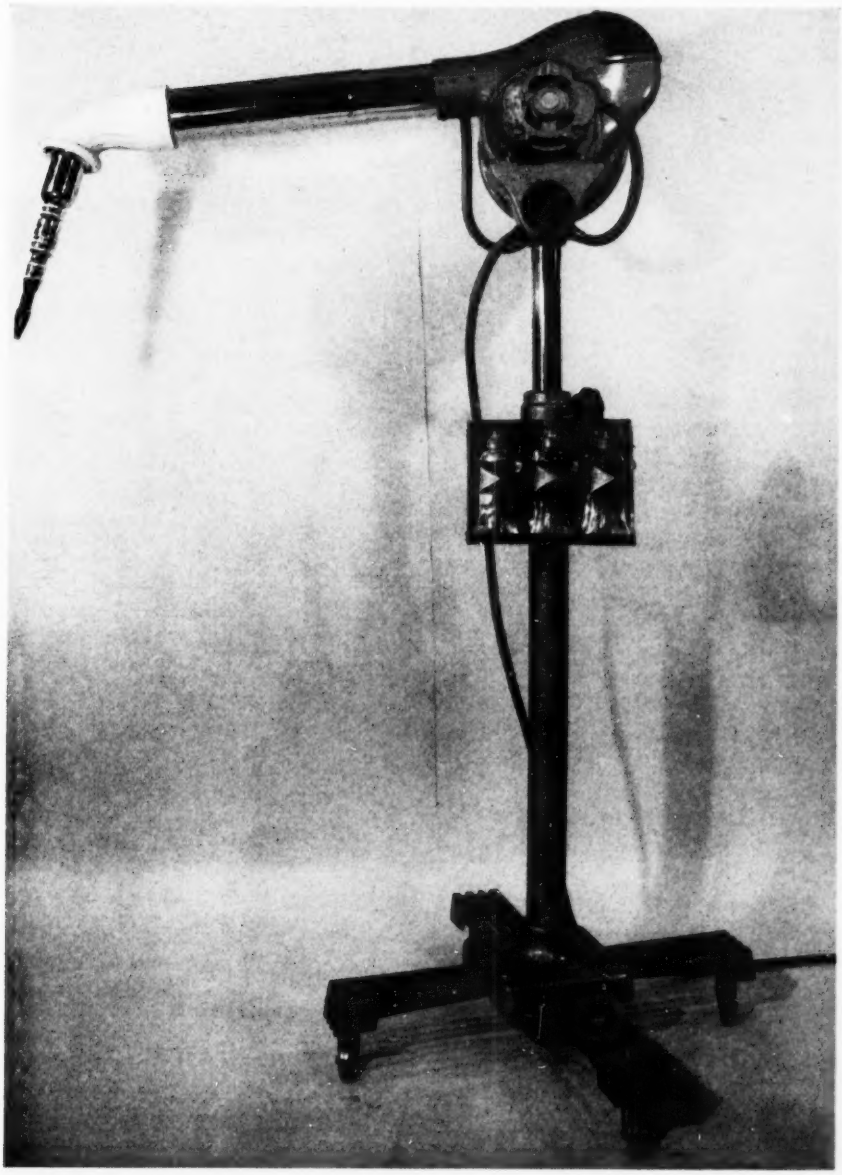

Fig. 2.—Mounted blower.

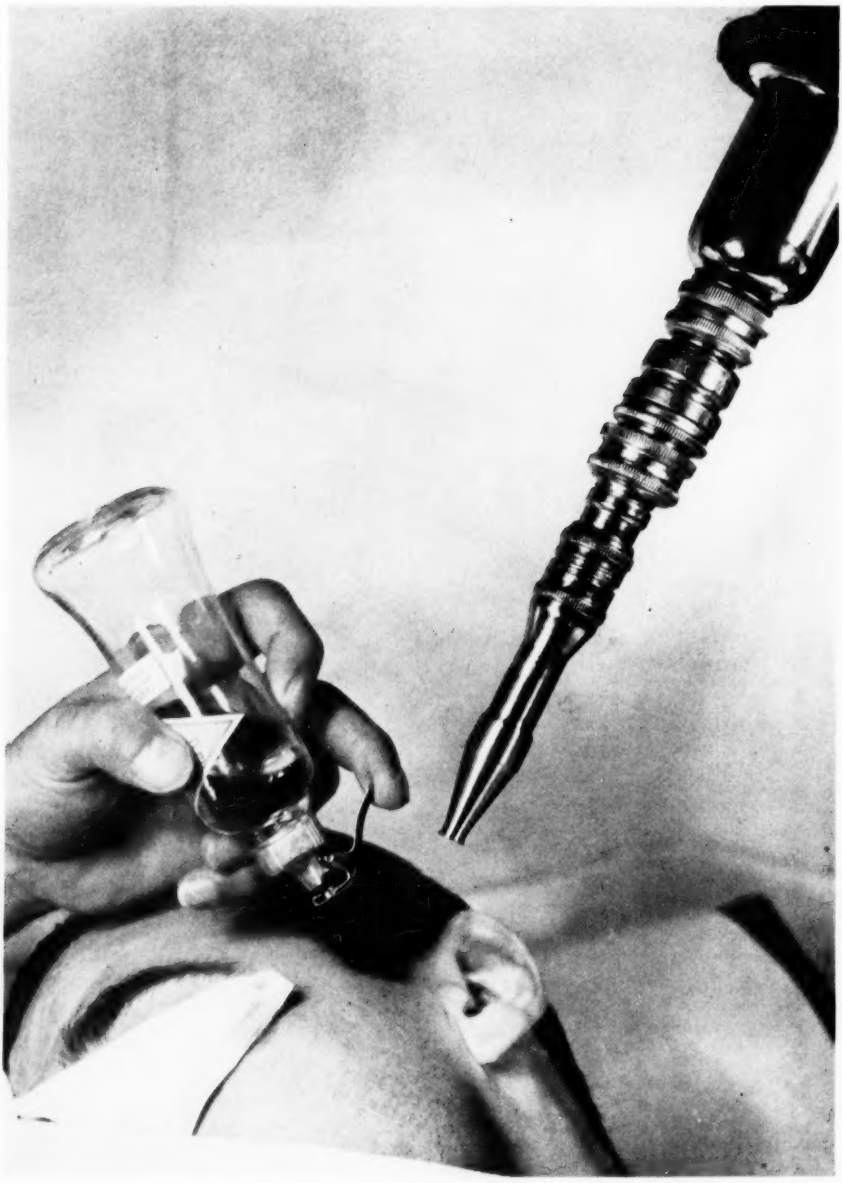

Fig. 3.—Relative positions of blower and ethyl chloride spray.

finger pressure should not indent the frozen skin. Three square inches (19 sq. cm.) are frozen at one time and treated individually, since experience has shown that an area this size can be adequately treated before thawing begins. The first sign of thawing is softening, followed by slight bleeding. The skin is still insensitive at this time, and further treatment is continued, if necessary, for a limited period.

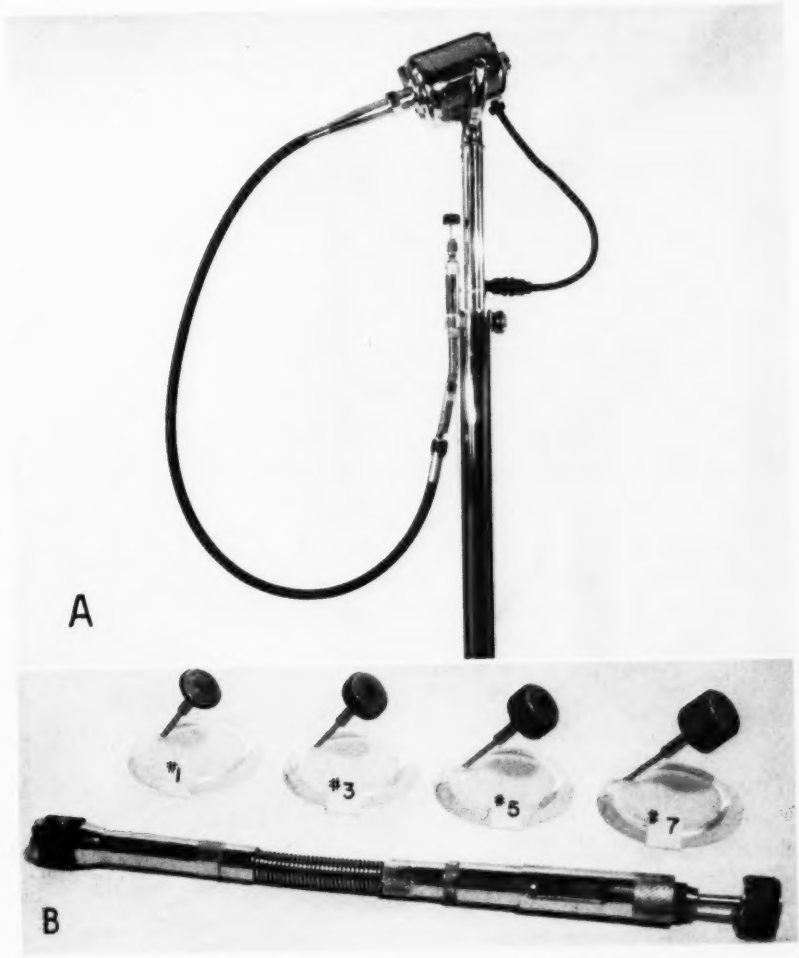

Fig. 4.—*A*, mounted planing instrument. *B*, detail of brushes.

Planing.—As a substitute for sandpaper, experiments were conducted with various types of motor-driven wire brushes. A wire brush abrades rapidly and may be applied selectively to small areas of the skin. Centrifugal force drives the abraded material in a particulate stream away from the field, and, thus, keeps the field and instrument free of epithelial debris. This stream is so heavy that it has been found necessary for the physician and the assistant to wear protective plastic clothing and face masks.

After testing a number of devices, the following apparatus is currently used.

The brush, ¾ in. (1.9 cm.) in diameter and 3/32 in. (0.238 cm.) thick, is made of stainless-steel wire which is 0.003 in. (0.008 cm.) in diameter.[3] Each strand is slightly curved in the direction of rotation. The brush is attached through a flexible hand piece and a 4 ft. (121.9 cm.) shaft to the mounted motor. The motor is 1/12 H.P. and rotates 12,000 times a minute. A rheostat foot switch permits variable speed control.[3]

The rotating brush is moved rapidly across the skin in a direction at right angles to the plane of the brush. This is important, because motion in the same plane as the long axis of the brush may result in grooving. Light pressure is maintained at all times. The rigid pit or elevation presents a guide to the depth of planing. Experience alone can dictate the depth and extent of planing at any one time. (Similarly, this experience has indicated if and when the procedure should be repeated. Usually, when indicated, it has been found possible to repeat treatment after four weeks.)

Postoperative Care.—A slight ooze of blood and serum starts after thawing and continues slowly for about 20 minutes. During this period the patient lies at rest under gauze packs. When the ooze has stopped a dry gauze dressing is applied, and the patient is dismissed with instructions to change the dressing within an hour. If the dressing is permitted to remain for a longer period, it will adhere to the wound.

Boric acid ointment was originally tried as a postoperative dressing. It caused persistent leakage from under the bandages and was therefore discontinued. Antibiotic ointments were also tested, but because of sensitization seen in two patients were also discontinued. Postoperative infection has not been observed, even after the use of dry nonantiseptic dressings.

Dressings are changed daily by the patient. Sterile gauze pads are employed. These are neatly held in position by Scotch tape. A crust forms in three days, and this usually separates spontaneously in a week. Rarely, a closely adherent crust will take a few more days to separate. This separation has been expedited by a gentle washing with warm water.

GENERAL RESULTS

In all cases, except one, healing occurred without complication. In this case, erythema of the treated parts persisted for several months and finally cleared. This may have been caused by excessive refrigeration.

The healed skin is soft and pliable. It is fresh in appearance and has shown no evidence of cicatrization. There has been no evidence of margination, and skin pigment has returned to normal in this entire series of white patients. Several darker-skinned patients of Latin descent have been treated, with no occurrence of pigmentary change.

The cases have been followed since March, 1949. The skin has remained well, and there has been no regression of appearance. Many of the patients treated have been observed for at least two years and confirm the observation on the permanence of the results.

SPECIFIC RESULTS

The following skin defects have been satisfactorily treated:

1. Acne scars. There has been treatment in 249 cases. Moderate acne activity is not a contraindication. It has been my experience that acne does not reappear in planed areas. This may be accounted for by "marsupialization" of superficial sebaceous glands. There are cases of resistant cystic acne, usually in the mandibular and neck areas, in which excellent response to this treatment is obtained. Hypertrophic ridging is easily flattened and heals smoothly. In the average acne case 2 to 4 planings have been required before maximum improvement was obtained. These have been done at monthly intervals.

2. Smallpox and chickenpox scars. In the two cases in which there has been treatment by me, both of scars of a severe nature, there has been response with almost total clearing. These scars are soft-walled, and only require one or two treatments.

3. Superficial epitheliomas. The large superficial multicentric epithelioma, difficult to treat by other means, can easily be managed. Treatment of one lesion of this type has been completed.

4. Keratoses. The senile and seborrheic type of keratosis can be fully removed. Ferric subsulfate (Monsel's Solution) may be painted on the treated area to prevent postoperative oozing.

Fig. 5.—*A*, acne scars before therapy. *B*, six weeks after first treatment. Despite all attempts at exact duplication of lighting, I believe that the follow-up photographs in this case and in the following cases are slightly prejudicial in my favor.

5. Tattoos. I have treated a severe accidental tattoo with excellent results. Art tattoos have also been removed. It is a difficult and tedious procedure, because much of the pigment is deposited in the corium. Some scarring will result, but, it remains, in my hands, the best treatment that I have tried thus far.

6. Wrinkles. Wrinkled skin responds in a remarkable way. Superficial wrinkles are easily removed. The regenerated skin is fresh and youthful looking. The accompanying figures, while showing the disappearance of wrinkles, do not adequately demonstrate the improvement of texture and color.

7. Keloids. These have been planed down to normal skin level and then treated by irradiation. At the present time, it is my preferred treatment.

8. Elevated and depressed scars (traumatic). These are easily planed and merged into the surrounding skin surface. Linear scars, so frequently seen after automobile injury, respond well.

9. Adenoma sebaceum. A case of severe adenoma sebaceum, in a man 40 years old, has responded very dramatically. Many tumors, the size of peas, numerous

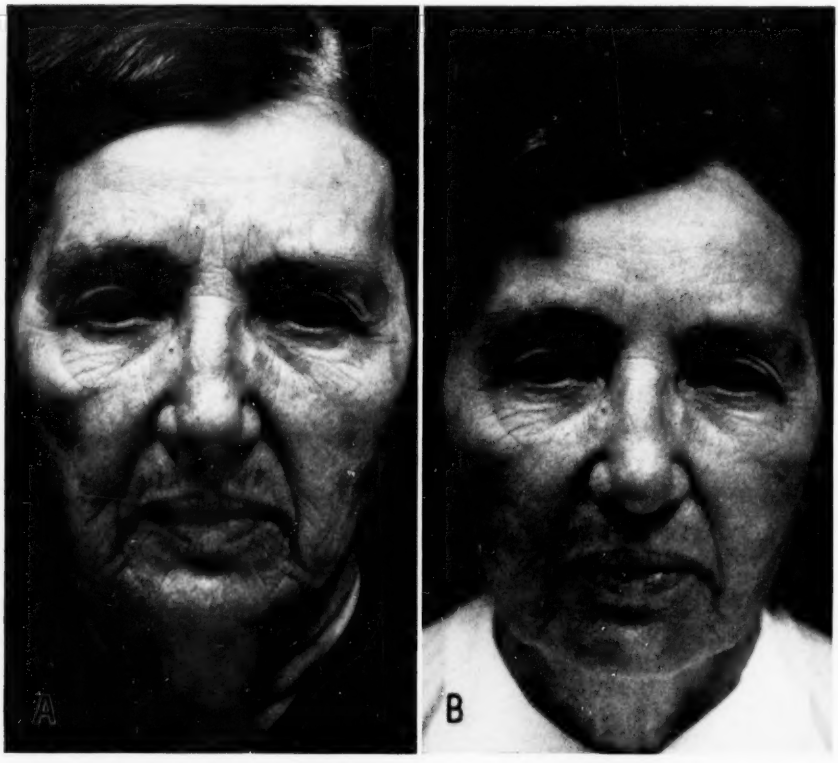

Fig. 6.—*A*, woman of 70 with generalized fine wrinkling. *B*, results two months after face was planed once. Because of the patient's age, only a small area was done at a time.

enough to be confluent over the entire face, were removed at one operation. Healing was normal. Only time can tell if the tumors will re-form.

10. Burn scars. This type of scar has been treated very lightly. The usual absence of hair follicles and the consequent lack of regenerative sites causes slow healing. The surface irregularities of the usual burn scar were markedly improved.

11. Nevi. Broad and linear nevi have been treated with good results. Vascular nevi also respond.

12. Lichenifications. Thick lichenified areas of neurodermatitis and lichen planus have been treated in this way. It is a rapid method for reducing the thickness of these lesions and thus making them amenable to other therapy.

COMMENT

It may take several hundred planings before the operator can develop a sense of dexterity and security. However, once the technique has been mastered, planing can be done rapidly as an office procedure.

The results reported depend upon the innate mechanism of skin healing. In the absence of infection, abraded skin tends to heal with a smooth surface, if this abrasion is not carried below the level of the hair follicles. It is my conclusion that fresh skin, the cells of which have not been genetically changed by years of exposure to sunlight, grows from these and presumably other multiple regenerative sites. At no time does the healed skin have the glazed, firm appearance of scar tissue. The number of treatments on any one area has been arbitrarily limited to four. The optimal intervals between treatments has been established by trial at about four weeks.

From the point of view of the patient, corrective surgical planing has been greeted by an overenthusiasm, even in those cases which, when viewed objectively, results have not been better than the usual 60 to 80% improvement. In many cases, despite pressure from the patient, further work was discontinued when it was felt that the magnitude of the procedure outweighed the possible benefits. The possibility of persistent skin irritability, caused by too many operations, as has been reported to have occurred after sandpapering, must be kept in mind.

945 Fifth Ave. (21).

MULTIPLE SUPERFICIAL EPITHELIOMATOSIS

Spectroscopic Study

WILLIAM A. ROSENBERG, M.D.
CHICAGO

MULTIPLE superficial epitheliomatosis is a term describing a form of primary carcinomata of the skin.[1] The disorder develops fairly early in adult life in persons exhibiting a marked tendency for multiple cutaneous neoplasms to develop. The lesions are usually limited to the trunk and face and consist of superficial scaly or crusting plaques having a very fine thread-like elevated pearly border similar to the rolled edge seen in basal-cell epithelioma. The plaques vary in size, and after many years' duration may be palm size or larger and may or may not metastasize.

Multiple epitheliomata are not infrequently seen as a manifestation in people who have had therapy with arsenicals [2] or exposure to arsenicals.[3] Some authors feel that arsenic is not completely exonerated even in those cases without therapeutic exposure, because occult exposure is practically universal.

Recently, I had an opportunity to observe and treat a patient with multiple superficial epitheliomatosis who had no history of treatment with or known exposure to arsenic. A spectroscopic analysis of some of the lesions was made for the presence of arsenic and other metals. Since I found no reference in the literature to such method of analysis, I thought it advisable to make this preliminary report.

REPORT OF A CASE

G. J. H., 64 years old, white, a streetcar motorman, was first seen on Oct. 13, 1951, for an eruption which had been diagnosed as psoriasis. At that time he stated that the disorder began 25 years ago as a single lesion on the left shoulder, followed several years later by another lesion on the right shoulder. Other lesions developed slowly, appearing on the back, chest, abdomen, shoulders, and right gluteal region.

The eruptions consisted of numerous nodules, pedunculated warts, and plaques. The nodules were smooth elevated pinhead-sized glistening lesions, varying in size from that of a pinhead to that of a split pea, and the plaques consisted of slightly infiltrated superficial well-defined reddish flat scaly lesions with pearly thread-like borders, varying from 1 to 8 cm. There were

From the Department of Dermatology and Syphilology, Chicago Medical School.

1. Ormsby, O. S., and Montgomery, H.: Diseases of the Skin, Ed. 7, Philadelphia, Lea & Febiger, 1948, p. 824.

2. Montgomery, H., and Waisman, M.: Epithelioma Attributable to Arsenic, J. Invest. Dermat. **4**:365, 1941.

3. Anderson, N. P.: Bowen's Precancerous Dermatosis and Multiple Benign Superficial Epithelioma: Evidence of Arsenic as an Etiologic Agent, Arch. Dermat. & Syph. **26**:1052, 1932.

no cutaneous evidences of either arsenical hyperpigmentation or arsenical keratosis. The patient said he had not taken any medication in the form of drops nor had he been exposed to arsenic.

Histologic Study.—The epidermis presented areas of thickening and of atrophy. There was a proliferation of basal cells extending outward into the stratum mucosum and downward both

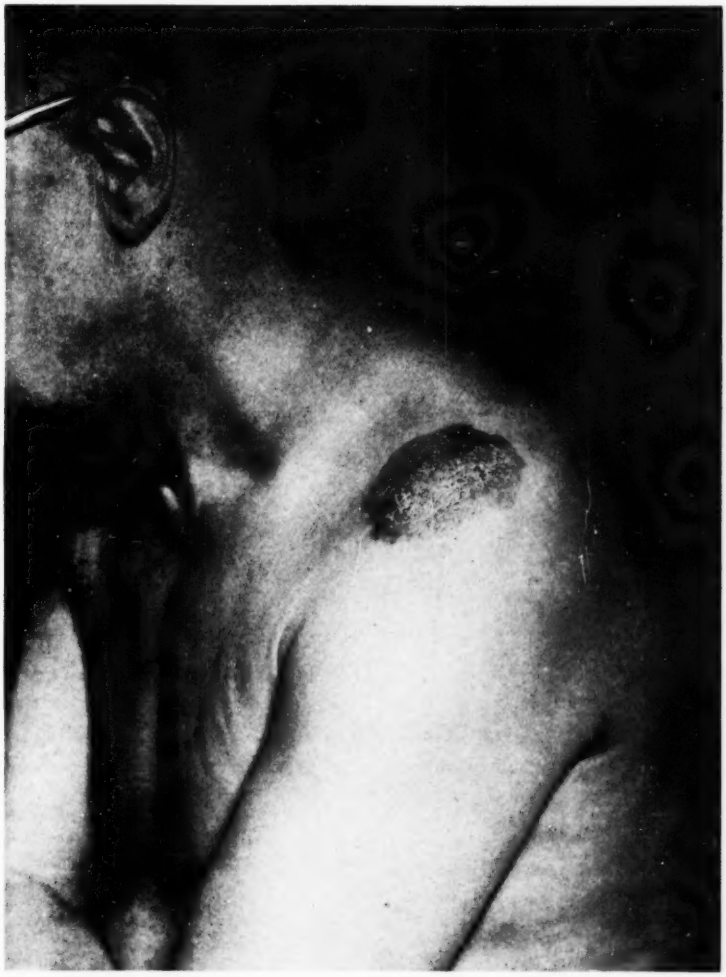

Fig. 1.—Superficial epitheliomatosis. Primary lesion, 25 years' duration.

as small buds and as larger masses of cells. The cellular component of these buds and masses resembled basal cells, varied in size, shape, and staining quality, crowded and irregular in distribution, and with a tendency to form a palisade arrangement at the periphery. There was a mild to moderate inflammatory infiltrate, consisting mainly of lymphocytes and plasma cells, extending throughout the upper portion of the dermis and around the tumor masses.

Spectroscopic Report.—Several lesions were excised and ashed, and these specimens were submitted to the Spectro-Chemical Research Laboratories, Inc., for a spectroscopic examination to determine the presence of arsenic and other metals. The laboratory report by Mr. Bernard B. Hauser is as follows:

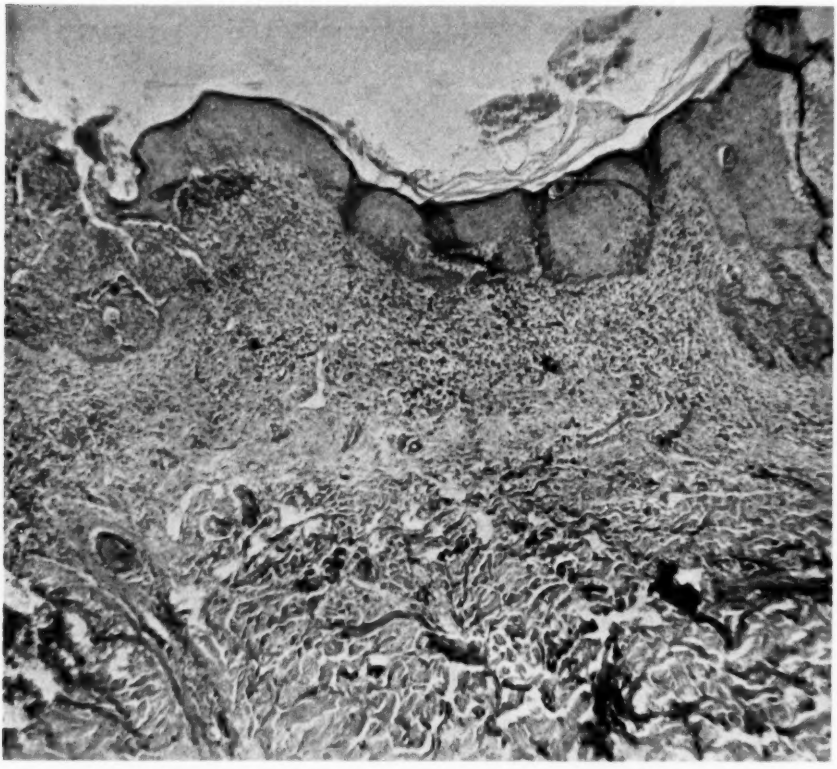

Fig. 2.—Basal cells proliferating outward in the stratum mucosum and downward as small buds and masses of cells.

Fig. 3.—Arrow points to missing line attributed to arsenic; two parts per million would be visible.

"Upon your request we examined spectrographically the submitted ashed sample. We use an A. C. arc, 5,000 volts, with a current of .3 am. Instrument used was an Applied Research 1½-meter-grating Spectrograph. Film used was Eastman Kodak Film No. 1. We exposed for 90 seconds and developed the film for three minutes in D 19.

"We found the following lines attributed to the presence of metals or metal salts in minute amount:

Major Constituent	*Wave Length*
Sodium	3302.99
Minor Constituents	
Phosphorus	2536
Iron	3021
Lead	2833
Copper	3248
Calcium	4227
Traces	
Manganese	2801
Magnesium	2852
Silicon	2882
Aluminum	3082
Titanium	3373
Silver	3281
Potassium	4047

"The test for arsenic gave a negative result. Two parts per million would be visible."

SUMMARY

This was a case of multiple superficial epitheliomatosis in which the history was negative for arsenic. To determine possible occult presence of arsenic a spectroscopic examination of lesions was made. The spectroscopic analysis employed was capable of detecting and revealing the presence of a quantity of arsenic in the specimens as minute as two parts in a million. No attribute of arsenic was recorded in the spectrogram. This method is suggested for further study as affording a more accurate, sensitive, and stable test to determine the presence of arsenic.

185 N. Wabash Ave.

ROLE OF COLLOIDAL OATMEAL IN DERMATOLOGIC TREATMENT OF THE AGED

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MINNEAPOLIS

SKIN PROBLEMS of the aged are receiving greater attention [1] since this age group comprises an increasing proportion of the total population. Many of the skin problems presented by the aged may be encountered in the younger age groups as well. Their occurrence, however, in a geriatric patient presents certain problems.

Blood vessels of the aging skin exhibit varying degrees of sclerosis, which interferes with the circulation of the organ. Atrophy of the epidermis occurs, which results in a flattening of the epidermodermal junction and in a slower regeneration of the epidermal cells. A modification of the subcutaneous tissue and varying degrees of atrophy of the cutaneous appendages occur. There is a loss of the elastic fibers and a degeneration of the collagen tissue, resulting in a thinner corium with less resilience. Wrinkles are the clinical manifestation of these changes.

Accompanying these histopathologic changes is a modified skin physiology. As with other organs in the aged, homeostasis is modified. The senile skin does not react as fast as youthful skin, nor do its reactions go as far. The skin is less able to control body temperature; there is a diminution of the activity of the sweat and oil glands, and the ability to restore and maintain the normal acid mantle is decreased. Inflammation is not as intense, and healing is prolonged. Pigmentation is more dense in the basal layers, and there is a localization of pigment, giving rise to the brown spots often referred to as "senile freckles." There is, however, a continued production of keratin, which, because of the decreased activity of the sweat and oil glands, is harder and more adherent. As the keratin thickens, senile keratoses result, and these, in turn, often become malignant.

The activity of the protective mechanisms of the skin—inflammation, weeping, sebaceous and sweat secretion—decrease in the aged. This skin with lower activity level and lower protective level often does not tolerate accepted remedies, and overtreatment dermatitis is a frequent consequence.

Underwood and Gaul [2] postulated that removal of the lipid film and consequent exposure of the horny mantle to the action of drugs was a predisposing factor

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From the Division of Dermatology, University of Minnesota (H. E. Michelson, M.D., Director).

This study was facilitated by the cooperation of Dr. Burton P. Grimes, Superintendent, St. Peter State Hospital; Dr. Nelsen P. Bradley, Superintendent, Willmar State Hospital, and their staffs.

1. Lane, C. G., and Rockwood, E. M.: Geriatric Dermatoses, New England J. Med. **241:** 772-777 (Nov. 17) 1949. Palmer, A. E.: Dermatologic Problems of Aging Women, Geriatrics **6:**363-379, 1951.

2. Underwood, G. B., and Gaul, L. E.: Overtreatment Dermatitis in Dermatitis Venenata Due to Plants, J. A. M. A. **138:**570-582 (Oct. 23) 1948.

to dermatitis. Sulzberger [3] reported that excessive use of soap removes the protective covering lipid mantle and temporarily prevents the reestablishment of the normal acid pH of the skin. This degreasing action is poorly tolerated by older persons.

The effects of soap upon the skin are often the underlying factors which predispose to varying dermatitis. The frequency with which this occurs is often underestimated.

The pH of normal skin is slightly acid, between 4.2 and 5.5. This acid mantle is protective against organisms and is important in maintaining the integrity of the armor-like keratin layer. Inflamed skin, on the other hand, is alkaline, the degree of alkalinity varying with the activity of the eruption. Soap, which has a pH of 9.5 to 10.5, removes the acid mantle.[4] The skin remains alkaline for some time until the acid mantle, produced in large part by the acidity of the sweat, can be restored. Since the activity of the sweat gland is decreased in the aged, senile skin seems slower in restoring the acid mantle.

To avoid the alkalinizing properties of soap, synthetic detergents with neutral or acid pH have been used.[5] These detergents very often prove to be too efficient, for they emulsify and remove the fatty acids on the skin, leaving it dry and often fissured.

Vegetable meals have been used empirically for a long time for both their cleansing and their therapeutic properties. It is indeed surprising that this practice is so widespread in view of the absence of any scientific literature on the subject. It would seem extremely worth while if a scientific basis could be established for this empiric therapy. The recent introduction of a specially purified colloid fraction of whole oatmeal for dermatologic purposes prompted this study.

EXPERIMENTAL STUDY

Colloidal oatmeal [6] is obtained by a special milling process involving separation of the colloid fraction from the whole-oat grain. The process is carried out entirely in the cold, in order to avoid any heat deterioration to the colloidal constitutents. The product contains 46% oat starch, 24% oat protein, and 9% oat oil.

It is a dry, palpable powder, stable under the usual conditions of storage, and is readily dispersible in both cold and warm water. The pH of varying test colloidal dispersions was determined in the usual manner with the Beckman pH Meter and is reported in Table 1.

The viscosity of the solution is a measure of the resistance to flow of the liquid and therefore would be indicative of the coating qualities. It is defined in terms

3. Sulzberger, M. B., and Baer, R. L.: Unusual or Abnormal Effects of Soap on the Normal Skin, in Medical Uses of Soaps, M. Fishbein, Editor: Philadelphia, J. B. Lippincott Company, 1946, Chap. 31, p. 51.

4. Bernstein, E. T.: Cleansing of Sensitive Skin, with Determination of pH of Skin Following Use of Soap and Soap Substitute, J. Invest. Dermat. **9**:5-9 (July) 1947.

5. Lane, C. G., and Blank, I. M.: Sulfonated Oil as a Detergent for Diseases of the Skin, Arch. Dermat. & Syph. **43**:435-443 (March) 1941.

6. Colloidal oatmeal used in this study was Aveeno and was supplied by the Aveeno Corporation, New York.

of force required to move one plane surface past another under specified conditions. It is expressed as a comparative measure, with the viscosity of pure water at 20 C. taken as 1. The viscosities of several concentrations of colloidal oatmeal were determined at body temperature.

The results reported in Table 1 indicate a high ability to cling to a surface as demonstrated by the increased force necessary to move a colloidal oatmeal plane past another surface (viscosity). The desirability of this is apparent when we consider that the longer an agent is in contact with the skin, the more efficient will be its therapeutic behavior. Thus, the tenacity of the colloidal oatmeal skin coating is highly desirable in order to counteract the alkalinity of the tissue exudate as well as the eroding action of clothing on the protective demulcent film.

The basic requisite of a skin buffer is the duration of effective action. This would be dependent upon the ability of the colloidal demulcent buffer to cling to the skin as well as the thickness of the residual film. The effect of perspiration is also important, since it is known that the acidity of the skin is dependent on the rate of evaporation of sweat; the more rapid the evaporation, the lower the pH.[7]

TABLE 1.—*The pH and Viscosity of Colloidal-Oatmeal Solutions*

Concentration *	pH †	Viscosity ‡
1:10	4.2	85
1:100	4.4	32
1:500	4.8	18
1:1,000	5.2	8
1:10,000	5.8	4

* Concentration by weight in distilled water.
† Measured with a Beckman pH meter at 20 C. using a calomel electrode.
‡ Centistrokes at 37.5 C. Water has a value of 1.

The volar surface of the forearm was washed with a dilute alkali solution, rinsed once with distilled water and patted dry. The pH of the skin was measured by the method of Bernstein[8] and the arm immersed in a dilute colloidal oatmeal (1:100) solution. The coated surface was patted dry and the pH values redetermined at definite intervals. The other arm was treated with alkali solution but not with the colloidal oatmeal and served as a control. The results reported in Chart 1 represent the mean values of 12 determinations carried out on three different days. Since both arms of the same person were used, they were subject to the identical physiological and thermal conditions, therefore compensating for the local effects of perspiration.

The pH buffering properties of colloidal oatmeal become rapidly apparent from an examination of the obtained data. However, in order to better translate these effects clinically, the pH buffering qualities against pathologic skin were determined.

The pH of skin exhibiting dermatoses was measured and treated with dilute colloidal oatmeal solution. The pH was then redetermined at regular intervals. The results reported in Chart 2 represent the mean of six determinations.

In order to evaluate further the effects of palliative therapy on dermatoses, colloidal oatmeal as a colloid bath[9] was used clinically with 139 patients. The patients were unselected and consisted of 53 women and 86 men, ranging in age from 21 to 91 years.

7. Blank, I. H.: Measurements of the pH of the Skin Surface, J. Invest. Dermat. **2**:67-74 (April); 75-79 (April); 231-234 (Oct.); 235-242 (Oct.) 1939.

8. Bernstein, E. T., and Herrmann, F.: Acidity on Surface of Skin, New York J. Med. **42**:436-442 (March 1) 1942.

9. Kierland, R. R., and Ede, M.: New Type of Colloid Bath, A. M. A. Arch. Dermat. & Syph. **63**:502 (April) 1951.

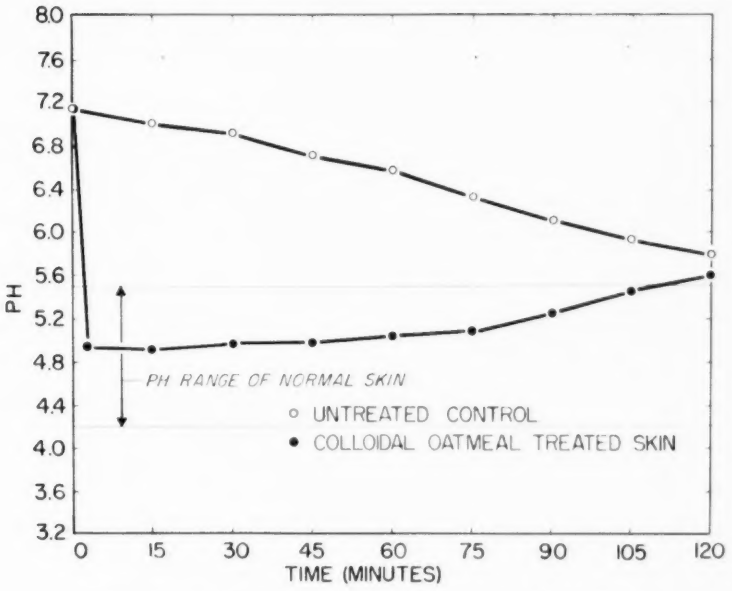

Chart 1.—Buffer action of colloidal oatmeal on alkali-washed skin.

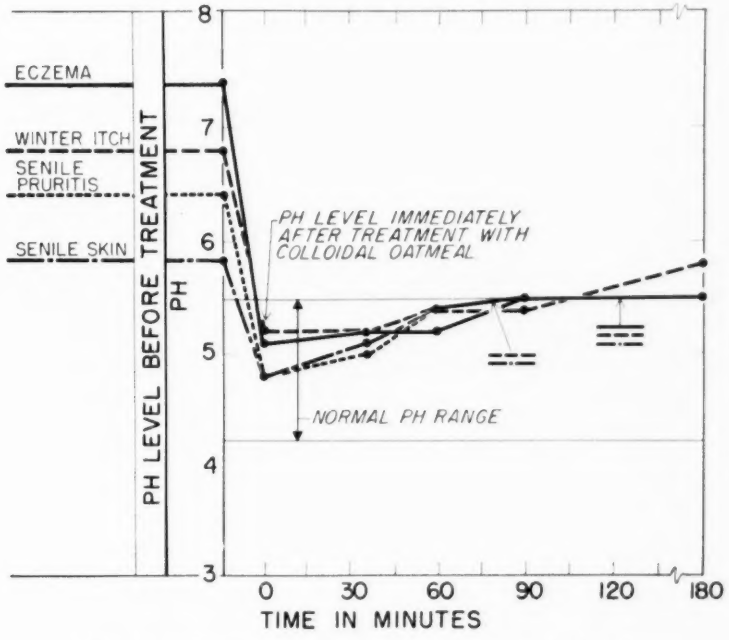

Chart 2.—Buffer action of colloidal oatmeal on pathologic skin.

The patients were instructed to use the colloidal oatmeal (1 to 2 cups) for the regular bath and as a skin cleanser. Soap was to be specifically avoided. No other topical therapy was employed, although drugs for internal use were permitted where indicated. In order to facilitate cleansing procedures, the following regimen was suggested:

The patients were instructed to wet the part of the body to be cleansed. Then they were to moisten the hands and pour 1 or 2 teaspoonfuls of Aveeno into them. They were to rub the oatmeal into a thin paste (using an additional small quantity of water, if necessary) and to apply and use like soap.

For those persons preferring the shower, the instructions were modified so that after a preliminary wetting of the skin, a solution of Aveeno is applied to the body with a massaging action. They were told to shower lightly, allowing the excess colloidal demulcent to remain on the body. The body should be patted dry.

The material does not produce a lather and is not as psychologically satisfying as soap. Most patients soon adjusted to this however, and many commented on the soothing quality of the baths. Some patients complained of a stickiness of the water-meal mixture. This stickiness was overcome by further diluting the

TABLE 2.—*Results Obtained with Aveeno-Colloid Baths in Dermatoses*

Indication	Patients, No.	Age Range	Results, Relief		
			Complete	Partial	No
Senile pruritus	46	51-99	33	11	2
Stasis dermatitis	33	44-84	19	11	3
Winter itch	33	21-81	24	8	1
Generalized ichthyosis with pruritus	9	32-85	9	..	..
Senile skin with dermatitis	14	65-91	11	3	..
Exfoliative dermatitis	2	31-52	2	..	..
Generalized pruritus	2	42-57	2	..	..
Total	139		100 (71.8%)	33 (23.7%)	6 (4.3%)

mixture. It should be noted that the demulcent properties make the bathtub slippery. A rubber mat or towel on the bottom of the tub will provide a more sure footing.

The patients were carefully followed for a three-month period and their progress noted.

Results.— The data reported in Table 2 need very little elaboration. Palliative demulcent therapy resulted in complete or marked relief in 71.8% of the group. Approximately 23% evidenced partial relief, while only 4.3% obtained no relief. The results obtained in patients complaining of pruritus were particularly impressive. Ninety patients of the series (64.8%) had a pruritic complaint. Of these, 68 (75.5%) evidenced complete or marked relief, 17 (18.8%) showed partial relief, and only 3 patients (3.3%) had no relief. Subjectively, the patients were much improved. Some patients reported that their skin appeared to be "softer" and more "silky."

COMMENT

A satisfying adjunct to this type of treatment is the lack of skin-sensitizing and nonirritating properties exhibited by this preparation. Very often the patient when finally seen by the dermatologist has already been subjected to a multitude

of topical preparations, which generally serve to inflame and irritate the primary process. Overtreatment dermatitis and its sequelae are perhaps the commonest complication of dermatological therapy.

By the judicious use of colloidal oatmeal as a colloid bath and as a skin cleanser, the inflamed skin is not irritated further and the inflammation of overtreatment is allowed to subside. Further, the buffering properties help restore the normal pH to the skin, healing processes are encouraged, and an early reversal of pathology becomes feasible.

SUMMARY AND CONCLUSIONS

The pH, viscosity, and buffer effect of Aveeno colloidal oatmeal on normal skin and pathologic skin was determined. The buffer action of Aveeno colloidal oatmeal produced an immediate and sustained pH comparable to that of normal skin, even after the skin was alkali-treated. Pathologic skin usually presents an alkaline reaction, and, therefore, similar physiological buffering activity may be expected clinically.

On the basis of the viscosimetric measurements, the tenacity of the Aveeno skin coating is of such nature as to counteract the alkalinity of tissue exudate as well as the eroding action of clothing on the protective demulcent film.

The clinical behavior of Aveeno colloidal oatmeal was evaluated in a series of 139 patients with common geriatric dermatoses.

Approximately 72% of the group obtained complete or marked relief, 23% evidenced partial relief, and only 4.3% obtained no relief. Many patients complaining of pruritus were relieved of symptomatology. Subjectively, the patients were much improved.

Aveeno colloidal oatmeal exhibited a remarkable lack of skin-sensitizing and irritating properties, making this agent valuable in avoiding overtreatment dermatitis.

The cleansing of soap-sensitive or irritated skin with Aveeno colloidal oatmeal proved very effective. Cleansing resulted without degreasing the skin.

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CORRELATION OF RATE OF GROWTH WITH HISTOLOGIC CHARACTERISTICS OF BASAL CELL CARCINOMA

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INTEREST in basal cell carcinoma of the skin has, in the past, been evidenced principally in studies relative to the histogenesis of the tumor.[1] Although isolated statements have been made concerning variations in biologic behavior, opinions have been empirical, based on clinical observation rather than on statistically proved data. The present study is concerned with attempts to associate biologic behavior of basal cell carcinoma with variations in histologic architecture.

Clinically, basal cell carcinoma may exhibit widely varying rates of growth. On the one hand, a small, circumscribed, nonulcerated lesion may have been present for a number of years and may well merit the term nevus or hamartoma.[1f] On the other hand, a lesion with a similar histologic picture may progress slowly but inexorably, with eventual invasion and destruction of large areas of tissue. Lack of ability to metastasize is, as yet, not satisfactorily explained.

REVIEW OF THE LITERATURE

Although previous studies on basal cell carcinoma have resulted in many morphologic classifications, these nosologic endeavors have been based purely on consideration of histologic variations, with few attempts at correlation with clinical behavior. Krompecher,[1a] in the first extensive pathologic study of the tumors, divided them into four groups: (1) those with a solid pouch-like downgrowth of epithelium; (2) epithelial masses containing cysts; (3) glandular forms, made up of interlacing strands of epithelial cells, and (4) tumors in which nests of epithelium form parakeratotic pearls. Most subsequent classifications have adhered to this concept with minor variations and elaboration.

Stout,[2] in a discussion of basal cell tumors, stated that nodular forms were extremely slow in growth and slow to ulcerate and therefore were of low-grade malignancy; these forms, as the basal cells accumulated in the skin, did not continue

From the Pondville Hospital (Massachusetts Department of Public Health), Walpole, Mass.

1. (*a*) Krompecher, E.: Beitr. path. Anat. **28**:1, 1900. (*b*) Mallory, F. B.: J. A. M. A. **55**:1513, 1910. (*c*) Haythorn, S. R.: Am. J. Cancer **15**:1969, 1931. (*d*) Foot, N. C.: Am. J. Path. **23**:1, 1947. (*e*) Teloh, H. A., and Wheelock, M. C.: Arch. Path. **48**:447, 1949. (*f*) Lever, W. F.: Arch. Dermat. & Syph. **57**:709, 1948. (*g*) Montgomery, H.: Radiology **25**:8, 1935.

2. Stout, A. P.: Human Cancer: Etiological Factors; Precancerous Lesions; Growth; Spread; Symptoms; Diagnosis; Prognosis; Principles of Treatment, Philadelphia, Lea & Febiger, 1932.

to penetrate the subcutaneous tissue but formed an elevated, hemispherical, epidermis-covered nodule in the skin. He likewise believed that tumors with differentiation toward sweat or sebaceous glands, hair follicles, and the like were never as aggressively infiltrative as undifferentiated basal cell growths.

Montgomery [18] grouped "basal cell epithelioma" into two categories, the benign and the malignant. The former included, in addition to unrelated types of tumors, epithelioma adenoides cysticum, syringoma, and cylindroma. The latter included basal cell carcinoma, basal-squamous cell epithelioma, and superficial epitheliomatosis. He considered basal-squamous cell epithelioma a true metamorphosis of basal cell to squamous cell epithelioma. Montgomery held the opinion that a basal tumor cell that retained its ability to form pigment was more differentiated and, therefore, less malignant than a basal tumor cell which multiplied without the formation of pigment.

Warren, Gates, and Butterfield [3] attempted to correlate the histologic type of tumor with the degree of radiosensitivity, the average diameter, the average duration, and the percentage of five-year cures. They concluded that the form of differentiation indicated the degree of malignancy; differentiation as a basal cell tumor or hair matrix indicated low malignancy, while differentiation toward epidermoid carcinoma indicated increasing malignancy.

Mackee and Cipollaro,[4] in a consideration of basal cell tumors containing prickle or squamous epithelial cells, stated that the course of this type is like that of a squamous cell tumor; it grows rapidly and metastasizes, and death is likely to result. In their opinion prognosis is guarded.

Eller,[5] in speaking of rodent ulcers, stated, "It may generally be said that the deeper the ulceration, the greater the degree of malignancy of the lesion and the tendency to rapid growth." He considered the pigmented basal cell tumor to be identical in behavior to ordinary basal cell carcinoma and considered unproved that an increase of cellular infiltration indicated a higher degree of malignancy.

Allen [6] disagreed with the generally held concept that a basal cell carcinoma with areas of squamous cell carcinoma represented a tumor with a poorer prognosis than the ordinary basal cell carcinoma. His experience did not support the concept that these tumors were prone to metastasize. He thought that it was much more reasonable to regard these areas of squamous cells as evidence of maturation of basal cells rather than as indication of dedifferentiation.

Willis [7] divided the basal cell carcinomas into those of superficial origin (rodent ulcer) and those of subepidermal origin. However, he stated that no sharp separation between basal cell growths of the superficial and of the deep type was possible and that growths similar in structure and behavior might arise from basal cells in any part of the epidermis and its appendages.

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3. Warren, S.; Gates, O., and Butterfield, P. W.: New England J. Med. **215**:1060, 1936.

4. Mackee, G. M., and Cipollaro, A. C.: Cutaneous Cancer and Precancer, Am. J. Cancer, 1937.

5. Eller, J. J.: Tumors of the Skin: Benign and Malignant, Philadelphia, Lea & Febiger, 1939.

6. Allen, A. C., in Anderson, W. A. D.: Pathology, St. Louis, C. V. Mosby Company, 1948.

7. Willis, R. A.: Pathology of Tumours, St. Louis, C. V. Mosby Company, 1948.

The only statistical correlation of histologic appearance with clinical behavior was presented by Lennox and Wells.[8] They considered four forms of differentiation: palisading, fluid formation, whorls, and pigmentation. They concluded that, "There are differences between the more and the less differentiated tumors, without reference to the type of differentiation; but these differences are relatively slight and of little importance in the individual case." Their analysis of the clinical behavior of tumors demonstrating each of these forms of differentiation revealed no differences. They noted, however, a gradation in behavior of rodent ulcers depending on the degree but not the type of differentiation. The differentiated tumors were less commonly noted on the face, appeared in younger patients, recurred less frequently, and responded better to irradiation than the undifferentiated tumors.

MATERIAL AND METHODS

The material for this study was derived from the pathologic files of the Pondville Hospital (Massachusetts Department of Public Health). Although consecutive examples of basal cell carcinoma were obtained from the files, many of them were discarded because of inadequate history of duration of the lesion or incomplete information about its size. Selection was based purely on the availability of an accurate history, an exact appraisal of the size of the lesion, and a technically satisfactory histologic preparation. Estimation of the size of the lesion was obtained from the clinical description, from the gross pathologic examination, and from examination of the histologic preparation. In case of discrepancy all three sources were considered, with emphasis on the last two. Estimation of size was based on measurement of the greatest diameter of the tumor; no attempt was made to estimate depth or total volume of tumor.

For purposes of statistical analysis, an index was obtained for each tumor, representing the ratio of the size to the duration of the tumor. Thus:

$$\text{Growth ratio} = \frac{\text{size of tumor in mm.}}{\text{duration of tumor in months}}$$

A tumor measuring 12 mm. in greatest diameter which has been clinically evident for 24 months would then have a growth ratio (G. R.) of 0.5. This technique involves some unavoidable inaccuracies. Thus, a clinical history of the duration of a cutaneous tumor is frequently inaccurate owing to the inconspicuous nature of the lesion, its long duration, and the forgetfulness of the patient. Clinical estimation of the size of a tumor includes only its visible and palpable limits; gross pathologic examination of a tumor likewise includes only an estimation of its visible and palpable limits; shrinkage of fixed material precludes accurate estimation of a lesion by measurement of the histologic extent of the tumor. Nevertheless, estimation of growth ratios compared favorably with the studies on growth of cutaneous carcinoma by Schrek and Gates.[9]

Each tumor was studied microscopically, and the following features were noted: squamous differentiation, peripheral palisading, cystic change, adenoid or pseudoglandular configuration, plexiform configuration, number of mitoses, degree of

8. Lennox, B., and Wells, A. L.: Brit. J. Cancer **5**:195, 1951.

9. Schrek, R., and Gates, O.: Arch. Path. **31**:411, 1941.

ulceration, character of the surrounding stroma, extent of adjacent inflammation, and degree of invasion. Mean growth ratios were determined for varying characteristics.

Significance of difference of mean growth ratios was determined by the formula

$$\frac{M_1 - M_2}{\sigma\,(M_1 - M_2)}$$

that is, the difference between two means divided by the standard error of this difference.

ANALYSIS OF DATA

Age.—The age distribution is noted in Table 1. Although the number of patients falling in the younger age groups is small, an increment in the mean growth ratio with increasing age is indicated, which is, however, not statistically significant. This fact corresponds with the generally held impression that basal cell tumors in young patients are usually slowly growing and resemble hamartial cutaneous growths in their biologic behavior, in contrast to the destructive tumors more frequently encountered in older age groups.

TABLE 1.—*Age*

Age, Yr.	No. of Cases	Mean Growth Ratio	Standard Deviation	Standard Error of Mean
20-29	3	0.10	....	....
30-39	4	0.40	....	....
40-49	11	0.95	0.66	0.20
50-59	14	0.90	0.48	0.13
60-69	30	1.42	2.25	0.41
70-79	31	1.29	1.47	0.26
80-89	7	0.62	....	....
20-59	32	0.78	0.60	0.11
60-89	68	1.28	1.78	0.22

Sex.—The overwhelming incidence of basal cell carcinomas in the male corresponds with existing knowledge. The mean growth ratio for 71 males was 1.12 (1.49), while the mean growth ratio for 29 females was 1.12 (1.61). No significant difference was noted.

Squamous Differentiation.—The tumors were divided into three general types: basal cell, mixed basoepidermoid, and basal cell with foci of keratinization. The mixed basoepidermoid carcinoma included tumors with large sheets of squamous elements which could be recognized as an epidermoid carcinoma in or associated with a basal cell configuration. The percentage of these tumors in this series is small, owing to rigid criteria for diagnosis. The basal cell carcinoma with foci of keratinization include many lesions ordinarily placed in the second group and characterized by small areas of squamous differentiation, parakeratosis, and occasionally formation of structures resembling abortive hair follicles. According to Lever,[11] the keratotic basal cell epithelioma represents a differentiated basal cell epithelioma with hair differentiation.

Although the values for mean growth ratios differ slightly, the differences are not statistically significant (Table 2). The tumors being divided into two groups as slowly growing and rapidly growing (Table 11), an arbitrary growth ratio of 0.7 was taken as the dividing line. Of the slowly growing tumors, 23.5% were basal

cell tumors with foci of keratinization, and 74.5% were simple basal cell tumors. Of the rapidly growing tumors, 32.7% contained foci of keratinization, and 61.2% were simple basal cell tumors. The number of pigmented basal cell carcinomas was too small for statistical evaluation. However, there was no indication that these carcinomas differed from nonpigmented forms. Likewise, the number of mixed basoepidermoid tumors was too small for statistical evaluation.

Peripheral Palisading.—Palisading of basal cells at the periphery of masses of tumor cells is a characteristic feature of the typical basal cell carcinoma. However, in a series of tumors, this characteristic may be present in varying degrees or may be completely absent. Of the slowly growing tumors (G. R. to 0.7), 62.7% showed this characteristic, in comparison with 63.3% of the rapidly growing tumors (G. R. 0.7 or more). Yet, consideration of mean growth ratios indicated an increment with disappearance of this histologic feature (Table 3). Although this difference is not

TABLE 2.—*Squamous Differentiation*

Tumor Type	No. of Cases	Mean Growth Ratio	Standard Deviation	Standard Error of Mean
Basal cell	29	1.37	1.89	0.35
Basal cell with foci of keratinization	67	1.03	1.38	0.17
Basoepidermoid	4	0.74	....	....

TABLE 3.—*Peripheral Palisading*

Degree of Palisading	No. of Cases	Mean Growth Ratio	Standard Deviation	Standard Error of Mean
0	13	1.92	2.07	0.57
1+	23	1.13	2.10	0.44
2+	44	1.08	1.18	0.18
3+	29	0.63	0.44	0.10

statistically significant, it may suggest the possibility that this feature is associated with less rapid growth.

Cystic Change.—The Brooks tumor, or epithelioma adenoides cysticum, is considered as a basal cell tumor with cystic change and is regarded as a tumor with little tendency to invasive behavior. Cystic change may occur in lower degrees in a significant percentage of basal cell carcinomas. Lever [1] considers cystic change as due to sebaceous differentiation in a basal cell epithelioma. Of the slowly growing tumors 35.3% showed some degree of cystic change, in contrast to 14.3% of the rapidly growing tumors. The mean growth ratios (Table 4) revealed a nearly significant difference in tumors showing cystic change, as contrasted with those in which cystic change was absent. The difference between the means of the two groups could occur by chance once in 60 times ($P = 0.016$).

Adenoid Configuration.—Many basal cell carcinomas assume a pseudoglandular, or adenoid, configuration, which has been interpreted by some as originating from sudoriparous glands and by others as apocrine differentiation of a basal cell carcinoma. The adenoid configuration was present in 27.5% of slowly growing tumors and in 16.3% of rapidly growing tumors. The mean growth ratios showed an increment, the difference of which, while not statistically significant when the extremes

were considered, might possibly bear further study (Table 5). A difference of this magnitude might be expected to occur by chance about once in 20 times. No significant difference in mean growth ratios was noted when the intermediate groups were considered. Thus the presence of an adenoid configuration suggests a slowly growing tumor which may be attributed to differentiation of basal cells or to fundamental differences in genesis.

Plexiform Configuration.—Occasionally the basal cells are elongated, spindle-shaped, and grouped in irregular, angular masses which appear to stream into the surrounding stroma. Peripheral palisading is almost invariably absent, and there is little attempt at cellular differentiation in the form of cystic change, adenoid change, or focal keratinization. Although this type of tumor gives an impression histologi-

TABLE 4.—*Cystic Change*

Cystic Change	No. of Cases	Mean Growth Ratio	Standard Deviation	Standard Error of Mean
Absent	75	1.29	1.57	0.18
Present	25	0.68	0.70	0.14

TABLE 5.—*Adenoid Configuration*

Degree of Adenoid Configuration	No. of Cases	Mean Growth Ratio	Standard Deviation	Standard Error of Mean
0	78	1.17	1.58	0.18
1+	14	1.07	1.55	0.41
2+	8	0.65	0.52	0.18

TABLE 6.—*Plexiform Configuration*

Plexiform Configuration	No. of Cases	Mean Growth Ratio	Standard Deviation	Standard Error of Mean
Present	23	1.58	1.67	0.35
Absent	77	0.98	1.44	0.16

cally of greater disorganization and possibly more unrestrained growth, no significant difference was detected in the mean growth ratios (Table 6). The plexiform configuration was present in 30.6% of the rapidly growing tumors and 15.7% of the slowly growing tumors.

Mitoses.—Abnormally large numbers of mitoses are characteristic of basal cell carcinoma. The increase in mitoses noted in histologic preparations is not consistent with the rate of growth noted clinically and has been attributed to delay or retardation of the mitotic cycle. Roughly quantitative mitotic counts were made enumerating the number of mitoses noted in an average of several high-power fields. No significant difference of the mean was noted in tumors with a low growth ratio as contrasted with those with a high growth ratio.

Ulceration.—Ulceration occurs in a large percentage of basal cell carcinomas of superficial type. In the subepidermal type, ulceration occurs much later and is secondary to epidermal pressure and atrophy. The possibility that the degree of ulceration might be an index of rapid growth was considered. Although a gradient

of mean growth ratios was obtained suggesting this possibility (Table 7), the difference, even in the extremes of degrees of ulceration, was not statistically significant. Of slowly growing tumors, 41.2% showed moderate or marked ulceration, as compared with 42.9% of rapidly growing tumors.

Stromal Type.—The stromal tissue surrounding the masses of basal tumor cells is characteristically loosely arranged and basophilic with ordinary stains. The stroma may be altered by the production of dense, fibrosed, and hyalinized connective tissue, which is compact and closely applied to the periphery of the basal cell masses. The stromal characteristics were divided into three types: (1) the typical thin, myxomatous, and basophilic stroma; (2) a much more dense collagenous type of stroma, and (3) a type intermediate between these two extremes. No statistical

TABLE 7.—*Ulceration*

Degree of Ulceration	No. of Cases	Mean Growth Ratio	Standard Deviation	Standard Error of Mean
3+	20	1.65	2.48	0.55
2+	22	1.11	0.91	0.19
1+	24	0.87	0.75	0.15
0	34	0.98	1.45	0.25

TABLE 8.—*Stromal Type*

Stromal Type	No. of Cases	Mean Growth Ratio	Standard Deviation	Standard Error of Mean
Dense fibrous	30	1.14	2.46	0.45
Intermediate	48	1.15	2.81	0.41
Myxomatous	22	0.96	1.35	0.29

TABLE 9.—*Inflammation*

Inflammation	No. of Cases	Mean Growth Ratio	Standard Deviation	Standard Error of Mean
Absent or slight	43	0.66	0.59	0.09
Moderate or marked	57	1.46	1.83	0.24

difference was noted in the distribution of lesions in the three categories, nor was there any significant difference in the mean growth ratio of each (Table 8).

Inflammation.—The inflammatory reaction may be interpreted as due either to secondary infection following ulceration or to attempts on the part of the body to limit the spread of the tumor. Many basal cell carcinomas contain a considerable surrounding inflammatory reaction in the complete absence of any surface ulceration. It is possible that the cellular reaction may be a manifestation of a protective reaction or of a response to rapid growth on the part of the tumor.

The difference in mean growth ratios between tumors showing no or only slight inflammatory reaction and those showing moderate to marked reaction is of sufficient magnitude to be of significance statistically (Table 9). The association of rapid growth with increase in inflammatory reaction suggests an inadequate tissue defense against rapidly proliferating tumor tissue.

Invasion.—Invasive capacities of basal cell carcinoma vary markedly in different tumors. The histologic picture may range from a well-localized subepidermal nodule,

which is well circumscribed, with no centrifugal spread, to a tumor which is widely and extensively invasive, with numerous foci of cells spreading to some distance from the primary cutaneous site. That this picture may be a valuable histologic criterion in the differentiation of slowly growing and rapidly growing tumors is indicated in Table 10. The difference between the growth ratios of tumors showing invasive tendencies and those lacking this feature is of sufficient magnitude to be statistically significant; i. e., a difference of this magnitude would occur by chance only once in 100 times ($P = 0.01$). Of slowly growing tumors, 64.7% showed no or only slight invasiveness, in contrast to 49% of rapidly growing tumors.

TABLE 10.—*Invasiveness*

Invasiveness	No. of Cases	Mean Growth Ratio	Standard Deviation	Standard Error of Mean
Absent	39	0.71	0.57	0.11
Present	70	1.29	1.69	0.20

COMMENT

Attempts at determining the degree of malignancy of tumors have been successful for epidermoid carcinomas and adenocarcinomas, and for some types of tumors grading can be correlated statistically with the prognosis of the type of tumor. However, in the case of basal cell carcinoma, the problem is much more difficult because of lack of clear-cut cellular characteristics indicating degree of differentiation of tumor cells. Also, the degree of mitotic activity is ordinarily related to the rapidity of growth of the tumor and is an important factor in determining the grade of the tumor. In basal cell carcinoma, mitotic activity apparently occurs independently of actual cellular proliferation or, at least, is not closely related to rapidity of cellular proliferation.

Regardless of one's concept as to histogenesis of these tumors, there are features exhibited by basal cell carcinomas which may be considered tentatively as evidence of differentiation of basal cells. On a theoretical basis, one might consider the following features as indicating attempts at differentiation: keratotic or parakeratotic areas simulating hair follicles; pseudoglandular, or adenoid, configuration, suggesting relationship to sudoriparous glands, and cystic areas. The last may be interpreted as evidence of sebaceous differentiation (Lever) or as simple central degeneration of tumor tissue. Peripheral palisading reminiscent of palisading of the basal layers of the epidermis is found in many tumors; its relation to differentiation is undecided but suggestive. The fact that these features (with the exception of keratinization) are noted oftener in slowly growing tumors than in rapidly growing tumors tends to support this hypothesis. Conversely, tumors which lack these characteristics, which show a marked surrounding inflammatory reaction, and which have a histologic picture suggesting invasion of surrounding tissue fall in the group of rapidly growing tumors and have a higher mean growth ratio. Although these differences in most cases do not meet the criteria for significance set up in this project, the probabilities of chance occurrence warrant further investigation of the problem. A measurable difference exists in the incidence of these features in slowly versus rapidly growing tumors; unfortunately, however, wide variations are encountered when individual tumors are considered. This wide variation and overlapping of

characteristics preclude accurate identification of the biologic type of individual tumors, such as one reasonably expects with the usual method of grading. Despite this defect, generalizations can be made, and further study of the basal cell carcinoma may result in more concrete information concerning the histologic characteristics identified with biologic activity.

SUMMARY

One hundred basal cell carcinomas of the skin were studied with reference to size, duration, and presence of various histologic characteristics. The mean growth ratio (size in millimeters/duration of tumor in months) was compared with histologic characteristics.

The slowly growing basal cell carcinomas showed a predominance of the following characteristics: occurrence in younger patients, presence of peripheral palisading, cystic change, and adenoid change. The rapidly growing tumors were characterized by a high incidence of marked inflammation and evidence of invasion of surrounding tissue. In most comparisons, the differences in mean growth ratios were not statistically significant but indicated the advisability of further study of the problem. A significantly greater degree of inflammation and centrifugal invasion was noted in rapidly growing tumors.

TABLE II.—*Histologic Characteristics of One Hundred Basal Cell Carcinomas of Skin*

Characteristic	Degree	% Cases to 0.69	% Cases 0.7+
Squamous differentiation	Mixed	2.0	6.1
	Basal cell	74.5	61.2
	With foci of keratinization	23.5	32.7
Peripheral palisading	0 to 1+	37.3	36.7
	2+ to 3+	62.7	63.3
Cystic change	Present	35.3	14.3
	Absent	64.7	85.7
Adenoid configuration	Present	27.5	16.3
	Absent	72.5	83.7
Plexiform configuration	Present	15.7	30.6
	Absent	84.3	69.4
Mitoses	0-4 per H. P. F.*	66.7	63.2
	5-8 per H. P. F.	23.5	22.4
Ulceration	0 to 1+	58.5	57.1
	2+ to 3+	41.2	42.9
Stromal type	Myxomatous	19.6	24.5
	Intermediate	47.0	49.0
	Dense fibrous	33.4	26.5
Inflammation	0 to 1+	47.1	38.7
	2+ to 3+	52.9	61.3
Invasion	0 to 1+	64.7	49.0
	2+ to 3+	35.3	51.0

* High-power field.

Miss Olive M. Lombard, Biostatistician and Research Associate in Cancer Control, Harvard School of Public Health, assisted in the statistical analysis and determination of probability rates.

ISONIAZID IN THE TREATMENT OF CHRONIC LUPUS ERYTHEMATOSUS

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CHRONIC lupus erythematosus is notoriously resistant to treatment. Until 1951, bismuth, gold, and arsenic were the principal systemic agents; second choices were suramin sodium (Naphuride),[1] quinine, crude liver extract, and vitamin E; third choice was local destruction, usually with carbon dioxide. In 1951, quinacrine (Mepacrine, Atabrine) was reported by Page[2] to have produced excellent results, and personal reports to us by several dermatologists indicate an increasing confirmation of good results in the United States. Any drug which offers help in the management of this disease is eagerly put to the test by those dealing with this discouraging condition.

Isoniazid was discovered to possess antituberculosis activity in vitro[3] and it produced dramatic effects in man[4] and in experimental animals.[5] Because tuberculosis was once thought to be associated with lupus erythematosus, gold was used in the treatment of both.[6] A relation between these two diseases is still under serious consideration,[7] and experimental work as well as careful postmortem studies

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1. Peck, S. M., and Klein, G.: Therapy of Dermatologic Disorders, Philadelphia, Lea & Febiger, 1951, p. 221.

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5. Grunberg, E., and Schnitzer, R. J.: Studies on the Activity of Hydrazine Derivatives of Isonicotinic Acid in the Experimental Tuberculosis of Mice, Quart. Bull. Sea View Hosp. **13**:3 (Jan.) 1952.

6. Schamberg, J. F., and Wright, C. S.: The Use of Gold and Sodium Thiosulphate in the Treatment of Lupus Erythematosus, Arch. Dermat. & Syph. **15**:119 (Feb.) 1927.

7. Ormsby, O. S., and Montgomery, H.: Diseases of the Skin, Ed. 7, Philadelphia, Lea & Febiger, 1948, p. 955. Kren, O., and Löwenstein, E.: Zur Pathogenese der Hauttuberkulose und der Tuberkulide einschliesslich des Lupus erythematodes, Wien. klin. Wchnschr. **44**:405 (March 27) 1931; cited by Layman, C. W.: Culture of Tubercle Bacillus by the Löwenstein Method, Arch. Dermat. & Syph. **28**:38 (July) 1933.

point to such a possibility.[8] The most recent trend of opinion, however, is away from tuberculosis.[9] The dramatic effect of the hydrazides of nicotinic acid on tuberculosis stirred the interest of dermatologists in their use for diseases associated with or related to tuberculosis.[10]

At the outpatient department for diseases of the skin at the Boston City Hospital, the seven patients here reported on were selected for treatment with isoniazid. Each patient was carefully studied to rule out the presence of tuberculosis as far as is possible by clinical studies; none showed evidence of this disease. The diagnosis of chronic lupus erythematosus was confirmed by biopsy in each case. No patient had any known contraindication to the use of the drug.

REPORT OF CASES

Case 1.—A. S., a man aged 54, had an eruption on the face, ears, and sides of the neck for 13 years. It had begun as typical lupus lesions on the cheeks; there had been a progressive increase in the size of the lesions and new lesions till four years before. The condition had been fairly stationary since then. No other serious illness was reported.

Previous treatment had consisted of administration of crude liver extract and bismuth subsalicylate by intramuscular injection; oxophenarsine hydrochloride (Mapharsen) intravenously; vitamin E by mouth and alpha tocopherol (Ephynal) acetate locally. None of these preparations produced any remarkable effect.

Cotinazin,[11] a brand of isoniazid, was given in tablet form, by mouth, 50 mg. three times a day, for 15 weeks. During the first week, the patient gained 3 lb. (1.3 kg.). By the end of the ninth week he was back to his pretreatment weight. He felt "wonderful," the itching had almost completely disappeared, the slow advance of the lesions seemed to have stopped, and, in his opinion, the lesions looked much paler. Objectively, the improvement, if any, was equivocal, although there seemed to be somewhat less intensity to the inflammation. Laboratory findings remained essentially normal.

Case 2.—S. G., a woman aged 37, had an almost completely generalized eruption of 15 years' duration. After starting on the face in a typical manner, the disease extended progressively and continuously, so that practically her entire surface area, except the palms and soles, was covered with lesions of chronic discoid lupus erythematosus in all the stages of metamorphosis from small, dark-red areas of acute inflammation to thin, pale scars with and without active borders and pigmentation. In the previous year, lesions had developed on the vermilion of her lips and inside her mouth. She had lost some weight; had intermittent, migrating joint pains; had occasional periods of low fever; had headache, fatigue, and loss of ambition and interest in life. Although her condition gave a strong impression of a chronic type merging into an acute or subacute disseminated phase, no laboratory confirmation of this situation was obtained. All the tests gave normal results. The blood count and the values for urea nitrogen, total protein, albumin, and globulin were normal. Only the erythrocyte sedimentation rate was moderately increased. No L. E. cells were found in the bone marrow or peripheral blood.

8. Becker, S. W., and Obermayer, M. E.: Modern Dermatology and Syphilology, Ed. 2, Philadelphia, Lippincott Company, 1943, p. 443.

9. Ormsby and Montgomery,[7] p. 957. Laymon, C. W.: Culture of Tubercle Bacillus by the Löwenstein Method, Arch. Dermat. & Syph. **28**:35 (July) 1933. Keil, H.: Relationship Between Lupus Erythematosus and Tuberculosis: Critical Review Based on Observations at Necropsy, ibid. **28**:765 (Dec.) 1933.

10. Editorial comment, in Year Book of Dermatology and Syphilology, edited by M. B. Sulzberger, and R. L. Baer, Chicago, The Year Book Publishers, Inc., 1951, pp. 87-89.

11. Supplied for this study by Dr. Elliott R. Weyer, of Chas. Pfizer & Company, Inc.

Previous treatment consisted of administration of penicillin, vitamin E, liver extract, and bismuth intramuscularly and of ferric cacodylate and gold intravenously. After a course of corticotropin (ACTH) she was much improved objectively and subjectively, but when use of the drug was discontinued the symptoms returned more intensified.

A 50 mg. of tablet of isoniazid was given three times a day for eight weeks. After three weeks, she felt stronger and more ambitious and was sure that the lesions were fading in color. Her joint pains disappeared, and her appetite was improved. At the end of eight weeks, she had gained 4 lb. (1.8 kg.). Objectively, her lesions had lost an appreciable degree of the redness of the areas which were most active, and some of the most recent lesions appeared less acute. The only side-effect evidenced was a slight hyperreflexia.

CASE 3.—J. T., a man aged 40, had typical lesions on the face, forehead, neck, upper chest, and back of four months' duration. The onset had been on the forehead. All laboratory studies gave results within normal limits except for an erythrocyte sedimentation rate of 18 mm. in one hour.

A 50 mg. tablet of isoniazid was given four times a day for five weeks. Within two weeks, most of the lesions were objectively improved; the color was fading, and infiltration and scaling were less. At the end of five weeks, some of the lesions had almost completely faded in the center, and the borders were paler and less palpable. However, a few new lesions had developed during the course of treatment. The only laboratory changes were a drop in the erythrocyte sedimentation rate from 18 to 3 mm. at the end of one hour and an increase in the eosinophiles in the peripheral blood from 2% to 5%. Impotence developed, use of the drug was stopped, and he recovered after several weeks.

CASE 4.—M. J., a woman aged 49, had numerous typical, depigmented scars of lesions scattered over her face. These were of eight years' duration. For the past nine months lesions had developed on and around her lips. After diagnostic x-ray examination of her teeth, her lips became very red, swollen, and tender, with a sensation of burning. The vermilion of the lips was edematous, tender, and superficially eroded; this condition extended beyond the vermilion onto the glabrous skin for about 5 mm., with adherent, small scales and light bluish-red crusts. Laboratory studies gave results within normal limits.

A 50 mg. tablet of isoniazid was given at this time, three times a day. After two weeks there was a decrease in the subjective symptoms. Because of nausea, administration of the drug was stopped for one week. The nausea subsided, and use of the drug was resumed, a 50 mg. tablet being given once a day for three weeks, and then twice a day for one week. All the subjective symptoms completely subsided; she felt better than she had before the treatment and her appetite improved. Objectively, the color had faded and the erosions were healed, but the scales and crusts were still present.

CASE 5.—A. M., a man aged 39, for three years had had several typical lesions of the lips and face; no activity had been manifested during the past two years, and he felt generally well. Laboratory studies gave results within normal limits. Previous treatment had consisted of administration of bismuth sodium triglycollamate (Bistrimate) by mouth, mapharsen intravenously, vitamin B_{12} intramuscularly, and cortisone ointment locally, all without effect.

Isoniazid in 50 mg. tablets was administered three times a day for three weeks without any improvement.

CASE 6.—A. N., a woman aged 52, for four years had typical lesions over the nose and cheeks; they were inactive and asymptomatic. Laboratory studies gave results within normal limits.

A 50 mg. tablet of isoniazid was given three times a day for four weeks. During the first five days the patient complained of headaches, but they subsided and there were no other untoward symptoms. She was "eating more than ever" and she felt better, although she could not describe how. There were no changes in the lesions.

CASE 7.—J. W., a woman aged 49, for six months had a typical, solitary lesion on the anterior chest. The lesion was about 2 cm. by 3 cm. in size; subjectively, it was itchy and burning. Laboratory study gave results within normal limits.

A 50 mg. tablet of isoniazid was given three times a day for four weeks. Objectively, there was no change in the lesion, but the patient stated that for the first time in six months the burning and itching sensation had completely subsided.

COMMENT

Isoniazid, a relatively new drug, used in the treatment of tuberculosis, was given to seven patients with chronic lupus erythematosus, of whom two had had disseminated and five had discoid lesions. All patients with subjective symptoms described improvement. In four cases (Cases 1, 2, 4, and 6), a definite increase in appetite and a feeling of well-being developed. In only two cases was there definite objective improvement (Cases 3 and 4); this was not, however, of any remarkable degree. Laboratory tests did not show any remarkable changes.

The only untoward symptoms which developed were transitory headache in one case (Case 6); nausea, which disappeared after reduction of dosage, in one case (Case 4), and impotence, from which the patient recovered, in one case (Case 3). Toxicity to this drug is not serious in man, according to the American Trudeau Society.[3] Whether these symptoms, in these cases, were causally related to the drug has not been positively established by us; we feel that it might be conservative to assume that there was such a relation.

Ninety patients with tuberculosis treated with isoniazid (a different brand from the one we used) at the Sanatorium Division of the Boston City Hospital, by Dr. D. S. Sherman, chief staff physician, had the following symptoms:

Vertigo: Very rare; first few days only.

Headache: Dull, frontal throb; seven cases; cleared in all after first or second week.

Drowsiness: Four cases; practically all patients slept better; 90% awakened with a start.

Hyperreflexia: Practically all cases; in 90% muscular irritability (general twitching).

Psychosis: One case; patient recovered on cessation of medication; no previous psychosis.

Euphoria: All patients became mildly euphoric; two became more aggresive.

Urinary stream delay; Three cases.

Mouth dryness: In a few cases; minimal degree.

Feeling of well-being: All except three patients felt better; all except the same three gained weight.

These 90 patients were resistant to streptomycin and paraaminosalicylic acid, and the isoniazid was given alone to practically all. The occurrence of such relatively mild side-effects confirms the reports of the American Trudeau Society of the low order of toxicity for this drug.

CONCLUSIONS

Cotinazin, a brand of isoniazid, was given by mouth to seven patients with chronic lupus erythematosus in doses of 50 mg. three times a day. The effect was similar to that produced in patients with tuberculosis, namely, a marked tonic and alterative effect. This almost obsolete pharmacological goal, formerly in such high fashion, seems here to be so clearly and objectively etstablished by clinical evaluation that it deserves serious consideration. Whether or not this drug has a specific chemotherapeutic action on tubercle bacilli has not yet been universally acknowledged. Robitzek, Selikoff, and Ornstein [4] believe that it does have such an effect. From the therapeutic action of this drug on the objective manifestations of chronic lupus erythematosus, no conclusions can be drawn about the possible relation to tuberculosis; no conclusion can be drawn as to its action on the etiological agent of chronic lupus erythematosus. The nonspecific results obtained justify a report and indicate a desirability of further study; there is an implication that its value may lie in the effect of an adjuvant.

PSEUDOAINHUM

Report of Congenital Case Involving Several Fingers and Left Wrist

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THERE occur in the medical literature descriptions of the pathological entity called "ainhum." Among the sporadic reports of this condition rare cases were described which were associated with diverse pathological syndromes.

True ainhum is a distinct condition. This strange word originates from the African term meaning "to saw."[1] It affects almost without exception the little toes of some adult Negroes. It is characterized by an initial grooved plantar callus which gradually encircles the affected toe, forming a sclerosing band that deepens and strangulates the digit with ultimate spontaneous amputation within 3 to 10 years.

Ainhum-like syndromes which are attributable to scleroderma,[2] trophoneurosis,[3] pityriasis rubra pilaris,[4] palmar and plantar keratoses,[5] syphilis,[6] leprosy,[7] cicatrices,[8]

Dr. Rudolf L. Baer, Associate Professor of Clinical Dermatology and Syphilology and Dr. Morris Leider, Assistant Professor of Clinical Dermatology and Syphilology assisted in the preparation of this paper.

This case has been presented at the meeting of the Long Island Dermatological Society, March 11, 1952, and the meeting of the New York Academy of Medicine, Section on Dermatology and Syphilis, May 6, 1952.

1. da Silva Lima, J. F.: On Ainhum, Arch. Dermat. & Syph. **6**:367 (Oct.) 1880.

2. Pavlovskaja, and Karischeva: Case of Sclerodermia Ainhumoides, Russk. Ztschr. Haut u. Geschlechts Kr. **10**:11, 1915. Sutton, R. L., and Sutton, R. L., Jr.: Diseases of the Skin, Ed. 10, St. Louis, C. V. Mosby Company, 1939, p. 588. Becker, S. W., and Obermayer, M. E.: Modern Dermatology and Syphilology, Ed. 2, Philadelphia, J. B. Lippincott Company, 1947, p. 779.

3. Matas, R.: The Surgical Peculiarities of the American Negro: A Statistical Inquiry Based upon the Records of the Charity Hospital of New Orleans, La., Decennium 1884-1894, Philadelphia, P. Dorman, 1896, p. 123.

4. (*a*) Stelwagon, H. W.: Treatise on Diseases of the Skin for the Use of Advanced Students and Practitioners, Ed. 7, Philadelphia, W. B. Saunders Company, 1914, p. 626. (*b*) Tatz, K.: Pityriasis Rubra Pilaris with Ainhum and Syringomyelia, Brit. J. Dermat. **58**:123 (May-June) 1946.

5. Unna, P. G.: Über das Keratoma palmare et plantare hereditarium, Vrtljschr. Dermat. **10**:231, 1883. Hyde, J. N.: A Practical Treatise on Diseases of the Skin for the Use of Students and Practitioners, Philadelphia, Lea & Febiger, Ed. 4, 1897, p. 598; Ed. 7, 1904, p. 608. Wigley, J. E. M.: Case of Hyperkeratosis Palmaris et Plantaris Associated with Ainhum-like Constriction of Fingers, Brit. J. Dermat. **41**:188 (May) 1929. Grschebin, S.: Observations on Ainhum: Does it Exist as an Independent Disease? Urol. & Cutan. Rev. **40**:98 (Feb.) 1936. Drummond, M.: A Case of Unusual Skin Disease, Irish J. M. Sc. **158**:85 (Feb.) 1939. Spinzig, E. W.: Ainhum: Its Occurrence in United States: Report of 3 Cases, Am. J. Roentgenol. **42**:246 (Aug.) 1939. Spencer, G. A.: Ainhum Associated with Hyperkeratosis Palmaris et Plantaris, Arch. Dermat. & Syph. **45**:574 (March) 1942.

(Footnotes continued on next page)

metabolic diseases,[9] syringomyelia, peripheral neuritis,[10] parasites,[11] keratoderma hereditaria mutilans,[12] ancylostomiasis,[13] a family disease,[14] and congenital anomaly,[15] as well as the result of known etiological factors, such as mechanical or thermal trauma or self-induced strangulation of digits with strings or rings for malingering purposes, must be sorted out from the entity "ainhum" and reclassified rather under a more appropriate term, e. g., "pseudoainhum."

The following report of a rare case of a congenital anomaly, simulating ainhum, is presented.

REPORT OF CASE

V. G., a white girl of Italian descent, was seen by me in consultation within the first hour of her birth, on April 2, 1945. According to the obstetrician, the child's mother, a secundipara was free from any pathological, serological, or physical abnormalities, aside from the fact that she had a unicornous uterus. The infant was delivered spontaneously. The placenta, amniotic fluid,

6. Wright, L. T.: Ainhum: Report of a Case Occurring in a Man with Syphilis, Urol. & Cutan. Rev. **28**:135, 1924. Butler, H. W.: Ainhum (Dactylolysis Spontanea), M. Clin. North America **9**:1187 (Jan.) 1936.

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8. Sutton, R. L., and Sutton, R. L., Jr.: Diseases of the Skin, Ed. 10, St. Louis, C. V. Mosby Company, 1939, p. 587.

9. Butler, H. W.: Ainhum (Dactylolysis Spontanea), M. Clin. North America **9**:1181 (Jan.) 1936. Shaffer, J. O.: Ainhum: Report of Case in Which Patient was White Woman with Diabetes Mellitus, Arch. Path. **43**:170 (Feb.) 1947.

10. (*a*) Tatz, K.[4b] (*b*) Findlay, G. H.: Ainhum, with Special Reference to Involvement of Fingers, Tr. Roy. Soc. Trop. Med. & Hyg. **44**:750 (June) 1951.

11. Horwitz, O.: Case of Ainhum Occurring in the Out-Door Surgical Department of Jefferson Medical College Hospital, Med. & Surg. Reporter **56**:649, 1887. Babler, E. A.: Ainhum, with Report of a Case, Ann. Surg. **48**:110, 1908. Castellani, A., and Chalmers, A. J.: Manual of Tropical Medicine, Baltimore, William Wood & Company, 1910, p. 1148.

12. Vohwinkel, K. H.: Keratoma hereditarium mutilans, Arch. Dermat. u. Syph. **158**:354, 1929. Wirz, F.: Keratoma hereditarium mutilans. (Zu dem Aufsatz von K. H. Vohwinkel), Arch. Dermat. u. Syph. **159**:311, 1930.

13. Eskridge, F.: Ainhum Complicating Uncinariasis Americana in an American White Girl, Med. Record **78**:492, 1910.

14. Duhring, L. A.: Case of Ainhum with Microscopic Examination by H. Wile, Am. J. M. Sc. **87**:150, 1884. Doyle, E. A. G.: Ainhum, Brit. M. J. **1**:1346, 1889. Wheatland, M. F.: Case of Ainhum, J. A. M. A. **45**:631 (Aug. 26) 1905. Weinstein, H.: Description of Ainhum, with Report of Interesting Cases Occurring in One Family, Proc. Canal Zone Med. Ass., Mount Hope, C. Z., **4**:110, 1911-1912. Simon, K. M. B.: Ainhum, a Family Disease, J. A. M. A. **76**:590 (Feb. 26) 1921.

15. (*a*) Proust, A.: Malformations congénitales rappelant l'ainhum, Gaz. d. hôp. **62**:369, 1889. (*b*) Schwalbe, G.: Die Morphologie der Missbildungen des Menschen und. Tiere, Pt. 11, p. 108 and p. 201. (*c*) Johnson, H. M.: Congenital Cicatrizing Bands: Report of Case with Etiologic Observations, Am. J. Surg. **52**:498 (June) 1941. (*d*) Bluefarb, S. M.: Constriction of the Finger Simulating Ainhum: Report of a Congenital Case, Arch. Dermat. & Syph. **57**:741 (April) 1948.

Fig. 1.—Seven and a half-year-old white girl with congenital pseudoainhum. Prenatal loss of the third and fourth fingers; ainhum-like grooves of the fifth finger and wrist of the left hand. The verrucae vulgares of a few weeks' duration disappeared spontaneously shortly after this photograph was taken.

Fig. 2.—Roentgen picture of the left hand showing absence of the distal and middle phalanges; the proximal phalanges of these fingers are almost entirely absent, with the exception of the epiphyses and the most proximal portions of the metaphyses. The rest of the bony structure of this hand is normal. Note soft-tissue constriction of wrist.

Fig. 3.—Congenital ainhum-like creases of the end phalanges of the third and fourth fingers of the right hand. Radial deflection of the end phalanx of fourth finger.

Fig. 4.—Maldevelopment of the distal phalanx of the right fourth finger. Note absence of the epiphysis and, in addition, the partial calcification, with probable fibrous union, of the body of this phalanx.

and amniotic membranes were apparently normal. Physical examination revealed a well-developed, healthy newborn infant, except for the following findings:

1. The middle and ring fingers of the left hand were missing, with only epithelialized pliable short tags being seen.

2. The little finger of the same hand presented a narrow smooth normally epithelialized groove encircling the midsection of the proximal phalanx.

3. The distal phalanges of the middle and ring fingers of the right hand also disclosed ainhum-like encircling grooves, in addition to a radial deflection of the distal phalanx of the similarly afflicted right ring finger.

4. A completely encircling, soft, smooth groove was present over the left wrist. No other defects were found on the lower extremities or on the rest of the body.

On successive semiannual examinations, no further changes were noted in the congenital defects, except that the amputation stumps of the left middle and ring fingers became leveled off i. e., the soft and pliable tags which persisted for a few months after birth were no longer in evidence as such, being gradually replaced by umbilicated depressions, without any evidence of gangrene or ulcerations as the rest of the hand grew larger. The other affected fingers and the grooves continued to grow proportionately with their underlying constituents.

On latest examination, October, 1952, the findings on the hands remained unchanged, i. e., without any impending complicating processes. The child is able to use both of her hands without any handicap.

The Wassermann tests of the mother's and child's blood gave negative results. Roentgen pictures, taken in January, 1952, show maldevelopment of the distal phalanx of the right fourth finger, with absence of the epiphysis and shortening of the distal phalanx. Incomplete calcification of the body of this phalanx, with probable fibrous union, is noted. There is a constriction of the middle phalanx in the distal joint, which is however, in the soft tissues, with the bony structure and joint appearing normal.

The left hand shows an absence of the distal and middle phalanges of the third and fourth fingers. The bodies of the proximal phalanges of these fingers are almost entirely absent, with the exception of the epiphyses and only the most proximal portions of the metaphyses. The rest of the osseous structures of the left hand appear normal. There is a constriction of the soft tissues in the region at the base of the left fourth finger. No osteoporosis or other bone pathology of either hand is present.

COMMENT

Wellman [16] discerned and rejected the diverse theories attributed to possible causes of true ainhum. He misinterpreted however, I believe, Proust's [15a] suggestion of resemblance between ainhum and congenital annular bands, because Proust did not propound that true ainhum is congenital in origin. His opinion was solely that the congenital annular bands may have possibly initiated the subsequent intrauterine amputations. He stated that if such amputations did not take place in utero, these anomalies usually do not progress after birth; they may affect an entire limb at any point, in either sex and in any race, and that fingers may occasionally be so affected.

Rouget [17] and also de Brun [18] did not accept the concept that ainhum and congenital amputations had anything in common. Jeannel's [19] opinion was that amniotic bands were not essential in the causing of congenital amputations, but maintained that some morbid alterations in the skin must have been the originators, for he found it difficult to understand how amniotic adhesions could otherwise be produced.

16. Wellman, F. C.: Criticism of Some of the Theories Regarding the Etiology of Goundou and Ainhum, J. A. M. A. **46**:636 (March 3) 1906.

17. Rouget, J.: Thesis, Paris, 1889.

18. de Brun, H.: De l'ainhum, Semaine méd. **14**:397, 1894.

19. Jeannel: Contributions á l'étude des sillons genitaux et des amputations spontanées, Arch. Tocol **3**:774, 1886.

He was also unable to explain why the depressions were always circular and not spiral, and why the amputations were not multiple. Raynaud [20] held a similar notion to Jeannel's. However, the absence of multiplicity of the so-called congenital amputations is not necessarily a fact. Johnson's case,[15c] which is singularly similar to my own, presented annular creases around some of the fingers of both hands and toes, one constricting band around the distal portion of the right leg, partial syndactylism of the fourth and fifth fingers of the right hand, and congenital absence of some of the toes. These deformities were noted at birth; the patient's father removed remnants of the left index and fifth fingers which were attached by fibrous strands to the proximal soft tissues of the left hand, shortly after birth, with scissors. This patient, a white man, 72 years old at the time of hospitalization, refused surgical intervention for the encircling scar-like fibrous constricting band of his right leg. He was apparently able to use both hands without undue difficulty throughout his life.

Ballantyne,[21] in his treatise on congenital amputations, also mentioned ainhum. He stated that the absence of the amputated part and the frequent absence of amniotic adhesions and bands, speak against traumatic amputations. He believed that such amputations are produced, or initiated, before the truly fetal period of prenatal life. He regarded congenital amputations as being teratological in their origin, belonging to the embryo rather than to the fetus. He also could not accept the thought that amniotic bands set up special pathological changes in the constricted part of the skin and thus led to annular amputations. In his belief, the disease and not the amniotic bands cuts its way to the tissue of the limb.

Streeter [22] and Schumann [23] shared Ballantyne's view, believing that the so-called "amniotic amputations" are in reality due to some trophic disturbance analogous to Raynaud's disease in later life. They emphasized that the fibrous amniotic bands, so-called, which pass from amnion to embryo appear to be the result of a local necrosis of the embryonic tissue, rather than that the amniotic derivatives caused the specific injuries. This theoretical explanation could be the most plausible one; however, the traceless absence of epiphysis from the terminal phalanx of the right fourth finger in my case demands a more concrete explanation.

The theory of Linzenmeier and Brandes [24] that premature loss of amniotic fluid is the cause of congenital deformities, such as annular grooves and amputations, is open to challenge.

Dock [25] suggested the possibility of an endocrine disturbance. There is no concrete evidence to support this view.

The belief that the umbilical cord may be the cause of congenital amputations is entirely out of the question. Since the cord is thicker than the digits of a fetus, the possibility of the cord encircling the fingers or toes, causing one or more amputations or annular creases, is too farfetched.

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20. Raynaud, L.: Amputations congénitales des doigts et des orteils rappelant l'ainhum, chez une kalyle, J. Mal. cutan. syph. **7**:193, 1895.

21. Ballantyne, J. W.: Manual of Antenatal Pathology and Hygiene, Baltimore, William Wood & Company, 1902, Vol. 2, pp. 396-397.

22. Streeter, G. L.: Contribution to Embriology, Washington, D. C., Carnegie Institution of Washington, 1930, Vol. 22, pp. 1-44.

23. Schumann, E. A.: Obstetrics and Gynecology, Philadelphia and London, Curtis, W. B. Saunders Company, 1933, Vol. 1, p. 481.

24. Linzenmeier, and Brandes: Extrachoriale Fruchtentwicklung und ihre Bedeutung für die Entstehung kongenitaler Deformitäten, Beitr. klin. Chir. **82**:100, 1912.

25. Dock, G.: Intra-Uterine Amputations, Tr. A. Am. Physicians **29**:528, 1914.

Beside Johnson,[15e] as far as I was able to ascertain, only Bluefarb[15d] described a case of congenital ainhum-like constriction which was not associated with some skin disease or other underlying pathological condition. In that report, the little finger showed an annular groove; shortening of the digital phalanges on another finger of the same hand was noted. No congenital amputations were present.

SUMMARY

A congenital pseudoainhum is reported in a healthy, well-developed, and, in all other respects, normal white girl. The defects are bilateral, involving five fingers, two of which were lost in utero. In addition, an encircling groove is noted over the left wrist. The grooves are smooth and pliable, in contrast to the condition found in true ainhum, as well as in the diverse ainhum-like entities.

Since the defects do not show any progressive alterations, i. e., the affected parts with their encircling grooves kept proportionally normal growth with the underlying structures for almost eight years, no further pathological sequelae are expected.

The literature was reviewed, with special attention given to cases of congenital annular creases and amputations of digits.

The causative factors of true ainhum, ainhum-like syndromes, and congenital pseudoainhum are still awaiting conclusive explanation.

ADDENDA

At the time that this paper was completed, an example of congenital annular soft-tissue constriction in an infant Negro girl was published in the A. M. A. Archives of Dermatology and Syphilology by Wells and Robinson.[26] Their case is similar to the one of Bluefarb,[15d] except that their photographs show multiple involvement, i. e., the left index finger, the right ring finger, and some of the toes. The roentgenograms did not reveal any bony changes, nor were amputations present.

The almost eight years of observation of my patient and Johnson's experience with a similar case[15e] substantiate Proust's statement that congenital annular bands do not further the pathological process after birth in this type of anomaly. "Prophylactic" surgery of encircling creases in the absence of other associated underlying pathological diseases of the skin is therefore of questionable value.

32-40 33rd St.

26. Wells, T. L., and Robinson, R. C. V.: Annular Constrictions of the Digits: Presentation of an Interesting Example, A. M. A., Arch. Dermat. & Syph. **66**:569 (Nov.) 1952.

INHIBITION OF TYROSINE-TYROSINASE REACTION BY MICROSPORUM AUDOUINI

Preliminary Report

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WHEN HAIR infected with Microsporum audouini is boiled in water to which a small amount of potassium hydroxide has been added, the fluorescent substance is removed and the remaining hair is lusterless and free from pigment. Spectrophotometric studies show a striking similarity between the spectra of hair infected with M. audouini and those of noninfected gray hair. These studies indicate that a chemical reaction occurs between the normal pigment of the hair and the invading fungus. In vitro studies show that melanin is produced by the action of tyrosine and tyrosinase, and that this reaction is inhibited by M. audouini or by the elaboration of some inhibiting substance produced by this organism when grown on artificial media (Table).

The liquid dextrose Sabouraud's medium used in this series of experiments contained: 1% Neopeptone; 2% dextrose; 0.2% agar, and 0.1% yeast extract. Twenty-five cubic centimeters was placed in each of six 100-cc. Erlenmeyer flasks, and to each container was added 25 mg. of tyrosine. Two of these flasks were inoculated with M. audouini-infected hair and two were inoculated with a four-day-old stock culture of M. audouini. The remaining two flasks were used as controls. After six days, all the flasks inoculated with infected material had produced characteristic colonies of M. audouini. When a satisfactory growth had been obtained, 1 cc. of tyrosinase solution (prepared by Seitz filtration of fresh potato juice) was added to the flask containing the growth obtained from infected hair, and 1 cc. was also added to the flask containing the growth which had been produced from the stock culture.

Within one hour following the addition of tyrosinase solution, the formation of dark brown melanin was complete in the flask which contained only the medium plus tyrosine. After six hours, a light tan color developed in the flasks which contained the fungus growths, but surrounding the growth in each of these flasks was a zone in which there was no pigment formation. This zone was most prominent in the flask in which the culture had been grown from infected hair. After 24 hours, the production of brown pigment in these two flasks had reached its peak, but the zone of color inhibition remained. This zone remained unchanged for six days.

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Part III of the paper read before the Section on Dermatology and Syphilology at the One Hundred and First Annual Session of the American Medical Association, Chicago, June 10, 1952.

Control tests with the medium alone, medium plus tyrosine, medium plus tyrosinase alone, and medium plus stock culture and infected hair were negative for pigment production.

The results of this experimental study suggest that there is an inhibitor substance produced by M. audouini when grown on artificial media which will inactivate tyrosinase (Table).

These results also suggest the theory that a similar substance is produced in vivo and that the inhibitor substance may diffuse through the hair contained within the follicle and affect the pigment-producing cells (containing tyrosine) in the scalp in the same manner.

Inhibition of Tyrosinase-Tyrosine Reaction by Microsporum Audouini

Flask	Content	Result
1	Medium; tyrosine	Control: no color change
2	Medium; tyrosine; stock culture	Control: no color change
3	Medium; tyrosine; infected hair	Control: no color change
4	Medium; tyrosine; tyrosinase	Melanin production complete in 1 hour
5	Medium; tyrosine; tyrosinase; infected hair	Zone of inhibition persistent 4 days
6	Medium; tyrosine; tyrosinase; stock culture	Zone of inhibition persistent 4 days

SUMMARY AND CONCLUSIONS

An inhibitor substance is elaborated by M audouini in infected hair and when grown on artificial media. This substance will inactivate tyrosinase and prevent the normal tyrosine-tyrosinase reaction (melanin production) as demonstrated by in vitro studies.

These preliminary experiments are to be repeated in more detail with use of mammalian tyrosinase. Other dermatophytes are also to be studied to determine whether they produce the same phenomenon.

ABSTRACT OF DISCUSSION

DR. STURE A. M. JOHNSON, Madison, Wis.: This is an excellent piece of basic research, and the authors are to be congratulated.

The work supports Kligman's observation (*J. Invest. Dermat.* **18**:231 [March] 1952) that infection starts within the hair follicle. One can readily see, therefore, why spot x-ray fails if only fluorescent areas are treated and why it is necessary to extract hair and look at the roots for fluorescence to insure cure.

Is hair capable of causing growth on a medium 400 days after removal also infectious to the human? This is an important health problem. At the same time one must remember that fluorescent hair is not always infectious. The insolubility of fluorescent material in well-known solvents should make us search for new vehicles for our fungicides.

Could it be that the prophyrins which inhibit M. audouini in the test tube might have therapeutic value? Although several vitamins, salts, and amino acids did not produce fluorescence, it might be that sugars, which produce good substrate pigment, will.

AXILLARY ODOR

Experimental Study of the Role of Bacteria, Apocrine Sweat, and Deodorants

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AND
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PHILADELPHIA

AS FAR back as history records, man has been aware of a distinctively malodorous scent that may emanate from his axilla. Since the axilla is remarkable anatomically for the presence of the apocrine gland, the unique body odor of this area has been popularly ascribed to this structure. Furthermore, racial differences in body odor have been related to differences in number of apocrine glands seen in the various races.[1] The intense acridity of body odor sometimes noted under stress situations is thought to be the result of apocrine sweating.

As a result of these speculations the apocrine gland has been thought of as a "scent gland," responding to emotional stimuli and thus performing the function of such similar glands in the lower mammalia. In studying the physiology of the apocrine gland[2] we have been impressed by the lack of appreciable odor in pure apocrine sweat as it initially appears on the skin surface. Moreover, it was noted that upon standing such sweat later developed a definite foul odor, which increased in intensity as time progressed. The realization of this fact prompted an investigation of axillary odor, with particular reference to the specific roles of bacteria, apocrine sweat, and deodorants.

I. THE ROLE OF BACTERIA

A. The Bacteriology of Apocrine Sweat.—The axilla, a moist, intertriginous skin site, contains maximal numbers of resident and transient skin micro-organisms. However, there is no knowledge of the bacteriologic state of apocrine sweat. As a prelude to the study of the role of bacteria in the production of axillary odor, it was necessary to determine what organisms, if any, might normally reside in the apocrine secretion.

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This work was supported (in part) by the Medical Research and Development Board, Office of the Surgeon General, Department of the Army (Contract Numbers DA-49-007-MD-154 and DA-49-007-MD-324).

1. Schiefferdecker, P.: Die Hautdrüsen des Menschen und des Säugetieres, ihre Bedeutung sowie die Muscularis sexualis, Zoologica **72**:1, 1922.

2. Shelley, W. B., and Hurley, H. J., Jr.: (*a*) Methods of Exploring Human Apocrine Sweat Gland Physiology, A. M. A. Arch. Dermat. & Syph. **66**:156, 1952; (*b*) The Physiology of the Human Axillary Apocrine Sweat Gland, J. Invest. Dermat. **20**:285, 1953.

Method: Twenty healthy men with no abnormalities of the axillae served as subjects.

1. Preparation of the axillae: The evening before the collection of the specimens, the axillae were closely shaved and cleansed thoroughly with Ivory soap. Again in the morning on arising, the axillae were cleansed with Ivory soap. Three hours later, immediately prior to collection of sweat specimens, the axillae were cleansed for a third time with Ivory soap. After rinsing, the axillae were swabbed with a pad soaked in 70% ethyl alcohol. Finally a 4 by 4 in. (10 by 10 cm.) Steri-Pad saturated with 70% ethyl alcohol was applied to the axilla and left in place for five minutes.

2. Collection of specimens of sweat: Upon removal of the alcohol-saturated Steri-Pad, a thin film of alcohol was seen on the skin surface. This was allowed to evaporate, and immediately afterward 0.15 cc. of a 1:1000 solution of epinephrine was injected subcutaneously to stimulate apocrine sweating. It is significant that eccrine sweating was not seen in these subjects during the collection period.

As soon as the apocrine sweat appeared, it was collected in a sterile capillary tipped glass pipette approximately 8 in. (20 cm.) in length. The dilated distal portion of the collecting tube was plugged with cotton in order to insure sterility. After the pure apocrine sweat was collected, the narrow capillary portion of the tube was dipped in a tube containing sterile petrolatum, thus sealing this end of the collecting tube to reduce evaporation of the specimen. The entire collecting tube then was placed in a large sterile test tube, capped with cotton, and promptly transported to the laboratory for bacteriologic study.

3. Methods of bacteriologic study: The contents of the fine capillary pipette were placed in 1 ml. of brain-heart infusion broth. Cultures were incubated aerobically and/or anaerobically. Hanging drop and Gram stain preparations were made of the broth cultures, and subcultures were made to nutrient agar and blood (horse) agar. When Gram-negative bacilli were present in the cultures, subcultures were also made to eosin-methylene-blue agar and SS agar.

The Brewer jar method was used in the anaerobic studies. Microaerophilic conditions were established with use of the Brewer jar method also, but the method was modified in that hydrogen was added, and the jar was not completely exhausted of oxygen.

Results: The bacteriologic study showed the following:

	Cultures		
	Aerobic	Anaerobic	Microaerophilic
Number of specimens	24	5	5
Number with bacterial growth	4	0	0

Of the four specimens which showed bacterial growth, two contained organisms of the genus Corynebacterium; one, of the genus Aerobacter, and one, of the genus Sarcina.

Comment: In spite of elaborate techniques and significant technical improvement, it is essentially true that complete and consistent sterilization of the human skin is practically impossible.[3] Bacterial counts can be significantly and even rapidly reduced, but because of the difficulty in protecting such a vast exposed organ, absolute skin sterility is as yet an elusive goal.

The only organisms grown in this study were common skin aerobes. These were of the Corynebacterium group, a normal resident of the skin surface, and two commonly found organisms, Sarcina (skin, air, soil, dust, etc.) and aerobacter (gastrointestinal tract, air soil, etc.), both of which may be found in the transient flora of the skin surface. We feel that their presence in the four specimens was the result

3. Blank, I. H., and Coolidge, M.: Degerming the Cutaneous Surface: Quaternary Ammonium Compounds, J. Invest. Dermat. **15**:249, 1950.

of accidental contamination of the apocrine sweat during collection. It is of interest that no anaerobes were found in apocrine sweat since sebum has been shown commonly to harbor such organisms (Propionibacterium).

Conclusion: Human apocrine sweat is normally a sterile fluid.

B. In Vitro Study of Axillary Odor.—With the knowledge that apocrine sweat was a sterile fluid as it initially appeared on the skin surface, an attempt was made to study axillary apocrine odors in vitro and to determine the role of the axillary flora in the production of this odor.

Method: Ten healthy Negro men were chosen for this study. No abnormalities were present in their axillae.

1. Preparation of the axillae: One axilla was prepared exactly as described above. The opposite axilla was unshaved and was not cleansed for at least 24 hours prior to collection.

2. Collection of the specimen: Collection of the specimen was identical with that described under bacteriologic study.

Ten microtubes (Tubes No. 1) were filled with pure apocrine sweat taken from the cleansed axilla, and 10 tubes (Tubes No. 2) were filled with pure apocrine sweat taken from the uncleansed axilla. In addition, another series of tubes (Tubes No. 3), especially prepared with a thin film of hexachlorophene in absolute alcohol lining the interior of the tube, were filled with pure apocrine sweat collected from the uncleansed axilla. All of these tubes were then allowed to incubate at room temperature and studied at varying intervals. Several similar specimens were kept refrigerated at 0 C.

3. Examination of the specimens: The specimens incubated at room temperature were then examined for odor in a careful, consistent manner at 1 hour, 6 hours, and 24 hours, then once daily up to the fifth day. Later examinations were made on the 8th, 11th, and 14th days. They were read in the same order at each examination, i. e., Tubes No. 1 (containing pure apocrine sweat from the prepared axilla); Tubes No. 2 (containing pure apocrine sweat from the unprepared axilla with hexachlorophene lining the interior of the tube); Tubes No. 3 (containing pure apocrine sweat from the unprepared axilla).

The tube was broken at the capillary end and then tested for odor by two examiners, and the results were recorded independently by each examiner, without knowledge of the other's reading.

Results (Fig. 1): No odor could be detected in any of the tubes at one hour after collection. In Tubes No. 1 no odor developed throughout the entire 14-day period. Tubes No. 2 had no perceptible odor until the final reading on the 14th day, when a faint odor was noted. Tubes No. 3 at six hours generated a strong odor which became very strong at 24 hours and remained at this intensity throughout the rest of the readings. In the refrigerated specimens no odor ever developed.

Comment: It should be emphasized that at one hour no odor was noticed in any of the tubes, as the graph indicates. This is to be expected, of course, if bacteria play any role in the production of the odor, since pure apocrine sweat was collected and the contaminant axillary bacteria would require an incubation period to produce this odor.

In the capillary tube, it may take longer for this odor to develop than in situ, since a smaller number of organisms may be present, or since in such a small tube the early odor changes might be below the threshold of our relatively insensitive olfactory organs.

The order in which the readings were made is significant, since it is possible that if Tubes No. 3 were studied first, the odor, which became intolerably strong on the second day, might have been followed temporarily by a period of anosmia.

It is interesting to note that on the 14th day there was some faint odor in Tubes No. 2, after all other readings of this tube had shown no odor. This would indicate that hexachlorophene had begun to lose its potency and that it was not entirely bactericidal but perhaps only bacteriostatic (at least for some organisms). Furthermore, it indicates that the axillary organisms were included in these specimens.

Of great significance is the fact that the odor developed in these tubes was, as far as we could tell, identical with the acrid axillary odor which we identify with the axilla of man. It is not surprising that the refrigerated samples failed to develop any odor, since the necessary bacterial activity would be absent under such conditions.

Summary: 1. Axillary odor was captured in the "test tube." It was produced within six hours after collection of pure apocrine sweat from an uncleansed, unshaved axilla.

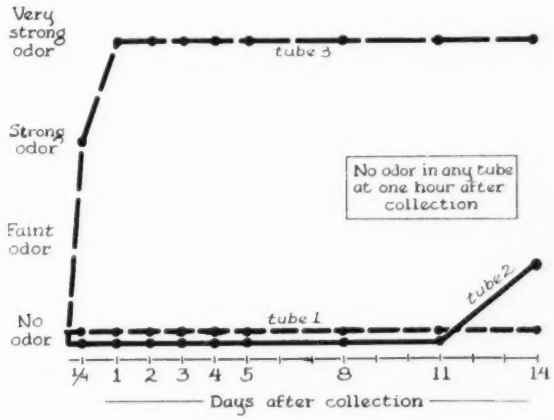

Fig. 1.—Effect of bacteria in development of odor in pure apocrine sweat. Tube 1 represents the series of tubes containing pure apocrine sweat from a "sterile" axilla. Note the absence of any odor. Tube 2 represents the series of hexachlorophene-coated tubes containing pure apocrine sweat from an "unsterile" axilla. No odor developed in these tubes until the 14th day. Tube 3 represents the series of tubes containing apocrine sweat from the "unsterile" axilla.

2. No odor was noted in the samples of pure apocrine sweat collected from the prepared "sterile" axilla even after 14 days.

3. The addition of hexachlorophene to a tube containing pure apocrine sweat from a normal unprepared axilla prevented any odor from developing until the 14th day, when a faint yet typical axillary odor was recorded.

Conclusion: Bacterial action is necessary for the production of odor from apocrine sweat. This experimentally produced odor is indistinguishable from the classical axillary odor seen in man.

C. In Vivo Study of Axillary Odor.—Although in vitro studies clearly indicated that bacterial action upon apocrine sweat would result in the typical body odor and that such odor could be prevented by removal or destruction of these bacteria, it was necessary to test this principle in situ; therefore an in vivo study was made of the effects of the use of a popular "germicidal" detergent on axillary odor and bacterial flora.

Method: Twenty-five healthy Negro men were chosen for this study and were divided into two groups of 10 (Group I) and 15 (Group II) men each. No abnormalities were present in their axillae, and axillary hair growth was good in all subjects.

Group I: 1. Preparation of the axillae: No shaving of axillary hair was done in these subjects. One axilla was carefully washed for five minutes with pHisoHex [4] once daily for seven days. The opposite axilla was also carefully washed for five minutes with pHisoderm once daily for seven days. Thorough rinsing of the axilla with tap water was done in each case following each wash, but no other soap, deodorant, or alcohol was applied to these areas during this trial period.

2. Examination of the axillae: These men were tested for the presence of axillary odor at 1-, 2-, 8-, and 18-hour periods. Subjects were placed in a supine position with their hands beneath their head and elbows directed laterally. Two examiners unaware of what the previous treatment had been carefully appraised these axillae for odor, each independently stating their findings to a recorder. A rest period of 10 minutes was allowed between readings. Readings were either negative (no odor) or positive (presence of odor), and no attempt was made to grade the readings. The odor of hexachlorophene, which was in itself pleasant, very faint, and easily distinguished from the classic axillary body odor, was recorded as negative (no odor), unless an axillary odor coexisted, in which case a positive reading was made. Differences in readings, when they occurred, were recorded as positive.

Group II: 1. Preparation of the axillae: The axillary hair was unshaved in these men also. For three days a daily five-minute wash with pHisoHex (to one axilla) and pHisoderm (to the opposite axilla) was done. Thorough rinsing of the axillae with tap water followed the washing, and no other soap, deodorant, or alcohol was applied to the areas during this trial period.

2. Collection of specimens: Two and one-half hours after the last axillary wash, 10 of these men were seen and placed in a supine position with their hands beneath their heads and elbows directed laterally. With sterile scissors and forceps, axillary hairs were removed from the respective axillae and placed on blood agar plates. Only one hair was placed on each plate. They were then incubated at 37.5 C. for 48 hours.

In the other five men, axillary hairs were removed and cultured in the same manner 20 hours after the last axillary wash.

Results: Group I. As is seen in Figure 2, the pHisoHex-treated axillae showed a significantly greater odor protection than the control axilla.

Group II: Of the hairs collected two and one-half hours after the last wash, none from the pHisoHex-washed side showed growth, whereas all of the hairs from the pHisoderm side showed luxuriant growth (Fig. 3).

In the test 20 hours after the last axillary wash, only one of five axillary hairs from the pHisoHex-washed axillae showed bacterial growth, while four of five pHisoderm-washed axillary hairs showed excellent growth after incubation at 37.5 C. for 48 hours.

Comment: It has been shown that pHisoHex [6] greatly reduces skin flora when used exclusively and repeatedly for cleansing. The effect of the hexachlorophene was revealed by using the same detergent base, pHisoDerm, as a control.

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4. pHisoHex is 18.4% hexachlorophene in pHisoderm, a water-miscible detergent preparation containing entsufon (sodium octylphenoxyethoxyethyl ether sulfonate), wool fat, cholesterols, and petrolatum. Both pHisoHex and pHisoderm are manufactured by Winthrop-Stearns, Inc., 1450 Broadway, New York.

5. Evans, C. A.; Smith, W. M.; Johnston, E. A., and Giblett, E. R.: Bacterial Flora of the Normal Human Skin, J. Invest. Dermat. **15**:305, 1950.

6 Dull, J. A.; Zintel, H. A.; Ellis, H. L., and Nichols, A.: Evaluation of pHisoderm G-11 and Liquid Soap Containing G-11 When Used as Preoperative Scrub, Surg., Gynec. & Obst. **91**:100, 1950.

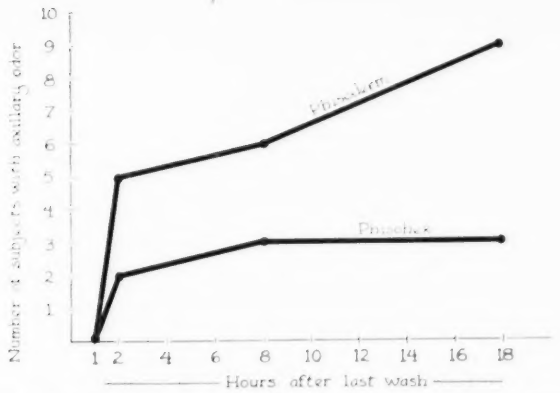

Fig. 2.—Effectivenes of an antibacterial-detergent preparation (pHisoHex) as an axillary wash in reducing axillary odor as compared with the detergent alone in the opposite axilla. The unshaved axillae of 10 men were washed once daily for seven days with the above preparations and examined for odor at the end of this time.

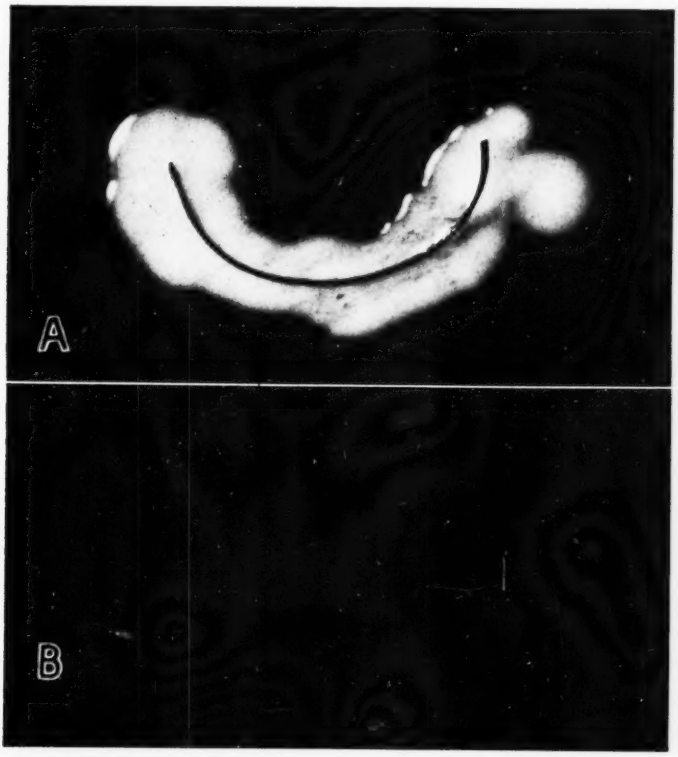

Fig. 3.—*A*, a hair which was was taken from the axilla of a subject who had daily axillary washes with pHisoderm for three days. Note the luxuriant bacterial growth on the agar plate, after 48 hours' incubation at 37.5 C. *B*, a similar hair from the opposite pHisoHex-washed axilla, in which no such growth is present.

It should be stressed that mechanical cleansing of the axilla is most important, and large amounts of antiseptics will hardly suffice in the absence of such cleansing. It is difficult to sterilize any skin surface, especially intertriginous sites, and diligent, thorough washes were, therefore, insisted upon in this investigation.

Conclusion: The use of pHisoHex in a daily five-minute wash resulted in the abolition of odor in seven subjects for as long as 18 hours as compared with abolition in two subjects using pHisoderm preparation. Concomitantly there occurred striking reduction in axillary bacterial flora as revealed by the study of representative hairs. This observation parallels the in vitro study on apocrine sweat and offers in vivo evidence that bacterial action is necessary for the production of body odor from the axilla.

II. THE ROLE OF APOCRINE SWEAT

The typical odor of the human axilla is certainly unique among the odors emanating from various body sites. Familiar to all of us, it has been attributed to the presence of apocrine sweat, but no direct studies had previously been made. Recent investigation of the physiology of the apocrine gland[2] have enabled us to examine aprocine sweat itself rather than mixed "axillary secretion" previously studied. Pharmacologic stimulation of the apocrine gland with epinephrine and immediate collection of the apocrine sweat droplets at their point of origin prevented any such contamination with other axillary secretions. In the earlier section of this paper it was demonstrated that normal apocrine sweat is initially sterile and odorless. Axillary organisms rapidly contaminate the sweat, and the classical axillary body odor developed in such unsterile specimens of pure apocrine sweat.

There is still further proof of the role of apocrine sweat in the production of axillary odor.

The endocrine system exerts a profound influence upon the apocrine sweat gland. The gland is undeveloped before the age of puberty and undergoes some degree of atrophy following the climacteric.[7]

It is known that children of the prepubertal age are without the classical axillary odor, and it has been shown that they do not produce apocrine sweat.[2b] It is believed also that many of the postclimacteric group have little or no such distinct odor. A study was made to see if there was a correlation between absence of odor and absence of apocrine sweat in elderly individuals.

Method: Five healthy men, ranging in age from 65 to 70 years were chosen for examination. The axillae were unshaved and unwashed for at least 12 hours prior to the examination. The patients were placed in a supine position, hands beneath their heads, with elbows pointing laterally and axillae exposed. Each was examined for axillary odor and was then given a test dose of epinephrine to stimulate apocrine sweating.

Results: Four of the five subjects studied showed the usual axillary odor. Those four also presented true apocrine sweat after adrenergic stimulation. The fifth subject, a 69-year-old white man, did not show the typical axillary odor, but rather a flat, somewhat vague scent. This patient also produced no apocrine sweat after stimulation.

Comment: The apocrine sweat in these four men was carefully examined and was identified with certainty according to the criteria elaborated previously.[2] These

7. Pana, C.: Recherche sulle variazioni strutturali delle ghiandole apocrine ascellari in relazione allo stato delle ghiandole sessuali e della mamella, Sperimentale **88**:580, 1934.

criteria were: (1) sweat was turbid white on the surface and in a capillary tube; (2) it dried to form a glistening glue-like cap; (3) it was follicular in location; (4) it appeared after an adrenergic stimulus. An equally thorough search for this secretion was made in the fifth subject, but none was seen.

Aprocrine sweat may be seen in the older age groups, as we have previously stated.[2b] However, there is no doubt that the amount is diminished just as the number of functioning glands is diminished. Yet even with minimal quantities, the essential substrate, namely, apocrine sweat, is available and will markedly influence the resultant odor of the area.

Conclusions: Aprocrine sweat is the necessary substrate for the production of the classic axillary odor of man.

III. OTHER FACTORS INFLUENCING AXILLARY ODORS

A. Axillary Hair.—The presence of terminal hair in the axillae is commonly regarded as an additional factor incrementing axillary odor. It is felt that retained

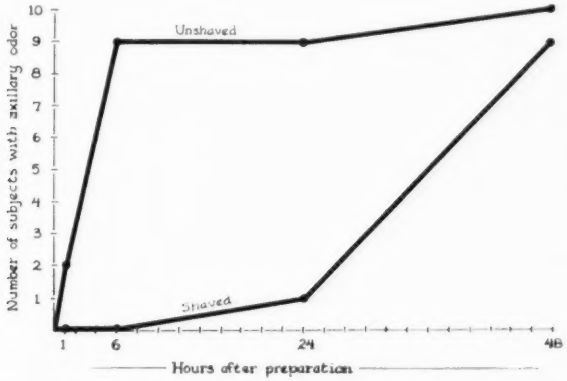

Fig. 4.—Effect of axillary hair in development of axillary odor. In 10 men one axilla was washed and shaved while the opposite axilla was washed but unshaved. Note the remarkable difference in the presence of axillary odor between the two sides.

axillary secretion and debris on the hair shaft act as an excellent medium for the growth of micro-organisms. Moreover, cleansing is made more difficult by the presence of such hair, and bacteria cling tenaciously to it. An attempt was therefore made to determine the influence of such hair in the development of axillary odor.

Method: Ten healthy Negro men were chosen for study. No abnormalities of the axillae were present.

1. Preparation of the axillae: One axilla was shaved and carefully washed with Ivory soap for 10 minutes. The opposite axilla was unshaved and was also washed with Ivory soap for 10 minutes. Each axilla was thoroughly rinsed with water.

2. Examination of the axillae: Olfactometric observations were then made in the same manner as previously described.

Results: In Figure 4 the results are clearly illustrated. The unshaved axillae of 2 men had a definite odor at the one-hour reading, and at six hours 9 of the 10

subjects showed such odor. At 48 hours all 10 of this group had the usual axillary scent. Contrast these with the shaved axillae, where no odor was detectable at 6 hours, and even at 24 hours only one man showed axillary odor. However, at 48 hours the shaved axillae of 9 of the 10 subjects showed the usual odor.

Comment: The very significant reduction in axillary odor in the shaved axillae substantiates the concept that retention of axillary secretion and bacteria will prompt an increase in odor.

It is apparent that the effect of this shaving was remarkable and was similar to the results of using pHisoHex in the unshaved axillae. It is understandable, therefore, that in women who regularly shave their axillae there is a markedly diminished axillary odor.

Conclusion: Axillary hair acts as a collecting site for axillary secretion, keratin, and debris, and favors bacterial growth and decomposition of such retained material. The removal of this hair results in marked reduction or elimination of appreciable axillary odor for as long as 24 hours.

B. Clothing.—Various authors[8] have stated that in odor to secure an odor-free area it is necessary to remove or reduce the surfaces upon which the secretions can cling. This is certainly true in the case of the axillary hair, as was demonstrated above. It also becomes apparent that clothing may play a similar role in odor production. Its influence in this process was investigated.

Method: Four healthy white men were chosen for this study.

1. Preparation of the axillae: The axillae were unshaved and were washed with pHisoHex for five minutes daily for one week. No special stimuli, emotional experience, or excessive exercise was encountered during this period, and no other soap, deodorant, alcohol, or other chemical was applied to the axillae. In all subjects eccrine sweating was normal and stained the shirt surface in the area. All wore clean white shirts during this study. Examination of the odor of the axillae and the shirts was then made at 1-, 3-, 6-, 12-, and 24-hour intervals.

Results: A great diminution of axillary odor was seen during this entire period.

It was noticed, however, that within two to three hours the definite body odor developed in the shirts at the site adjacent to the axillary skin. This zone was stained by axillary secretion.

Comment: The practical significance of this study is immediately appreciated. While we may with various techniques approach sterility in the axilla and thus remove odor of this area, it is true that bacteria normally reside on adjacent clothing and when the substrate, i. e., apocrine sweat, is present, the necessary decomposition will occur and odor will develop. Thus, even if the axilla is odorless, some odor can develop from the adjacent clothing. This is especially true if apocrine sweating is excessive, since obviously large amounts of the required odor substrate, apocrine sweat, will be available.

Conclusion: Clothing will definitely aid in the production of axillary odor, since organisms may cling to this clothing along with the axillary secretion and then result in bacterial decomposition and subsequent odor production.

8. Hollander, L.: Deodorants—Facts and Fallacies, Pennsylvania M. J. **49**:971, 1946. McCord, C. P., and Witheridge, W. N.: Odors—Physiology and Control, New York, McGraw-Hill Book Company, 1949.

C. Eccrine Sweat.—It has been said that eccrine sweat is a sterile, odorless fluid upon secretion.[9] Furthermore, it has been claimed that after the sweat stands for several hours an odor will develop,[10] presumably because of bacterial action. However, the collection techniques employed in these studies did not allow for an accurate study of pure eccrine sweat, since the samples were contaminated with keratin, debris, sebum, apocrine sweat, or hair. It is apparent that the study of the odors of pure, normal eccrine sweat depends upon a collection of uncontaminated specimens. In the present investigation appropriate techniques were employed to permit collection of such uncontaminated eccrine sweat.

Method: Profuse thermal sweating was induced in a normal healthy man in whom the axillae had been thoroughly cleansed and shaved. Uncontaminated eccrine sweat droplets were collected from the axillae in the small glass pipettes in the manner described earlier. It should be stressed that the secretion was absolutely clear and watery in consistency.

Two sets of five tubes each were collected, viz., Tubes A, containing pure eccrine sweat; Tubes B, containing pure eccrine sweat and with a thin film of hexachlorophene lining the interior of the tubes.

In addition, small vials of contaminated eccrine sweat were collected from the trunk, legs, and neck. A "scraping" technique, that is, running the mouth of the vial along the skin of these sites, was used. The fluid in these vials was not clear, but was turbid white in appearance. These tubes were then incubated and were independently examined for odor at 2, 24, 48, 72, and 96 hours by two investigators.

Results: It was found that no odor whatsoever developed in any of the tubes of pure eccrine sweat that were collected from the axillae.

Appraisal of the small vials containing contaminated eccrine sweat from the trunks, legs, and necks revealed that a distinct odor was present at 48 hours. This odor was not pungent or at all offensive and was markedly different from the "axillary odor" previously developed in vitro. This odor increased slightly in intensity at the end of 96 hours. These specimens were cultured for bacteria, and all showed definite heavy growth both in brain-heart infusion broth and on blood agar plates in 48 hours.

Comment: It is almost impossible to properly evaluate the specific roles of body secretions in the production of odor unless one is able to selectively study the secretion itself. Such contaminants as keratin, sebum, and debris could be responsible for odor development per se and could, therefore, mask the primary odor.

It seems apparent that eccrine sweat is of no importance as a primary odor source. However, it would seem that a definite function might be ascribed to this secretion in the production of axillary odor. Aside from the obvious impetus to bacterial growth it affords, eccrine sweat might also aid in the volatilization of the odoriferous products of bacterial decomposition; thus, the apparent "flush" of odor at an emotional crisis, when emotional eccrine sweating occurs. Fresh apocrine sweat, while odorless when it initially appears on the skin surface, could also aid in the volatilization process.

9. Eller, J. J.: Body Odor, M. Rec. **154**:167, 1941.

10. Kilian, J. A., and Panzarella, F. P.: Comparative Studies of Samples of Perspiration Collected from Clean and Unclean Skin of Human Subjects, Proc. Scient. Sec. Toilet Goods & A. **7**:3, 1947. Bergeim, O., and Cornbleet, T.: The Antibacterial Action of the Lactic Acid and Volatile Fatty Acids of Sweat, Am. J. M. Sc. **205**:785, 1943.

Conclusion: Uncontaminated eccrine sweat has no perceptible odor, whether sterile or unsterile. The addition of bacteria and of contaminants such as keratin, sebum, debris, apocrine sweat, and hair to eccrine sweat is necessary for the development of any odor. Such odor is rather vague, flat, and indistinct, and totally unlike that generated from apocrine sweat.

IV. THE ROLE OF ANTIPERSPIRANT-DEODORANT PREPARATIONS

Investigation of axillary odor almost inevitably leads to a study of the effects of antiperspirant-deodorant preparations. Such substances are used regularly by a vast proportion of the American public, yet their mechanism of action is not entirely clear.

A. Antiperspirant Activity of the Aluminum Salts.—Sulzberger, Zak, and Herrmann [11] showed histologically in biopsy specimens from the axilla that aluminum chloride preparations may produce periductal inflammatory changes which result in eccrine duct occlusion. They implied that a resultant diminution of eccrine sweat is produced at the skin surface. It is admitted that not all of the sweat glands of the area are rendered functionless, and that only a partial anhidrosis would result. We have attempted to determine whether a significant reduction in the amount of eccrine sweating could be demonstrated physiologically.

Sulzberger and his associates [11] also stated that a degenerative change occurred in the apocrine tubular cell after the repeated use of aluminum chloride preparations. Again their studies were limited to the histologic approach.

From the clinical test standpoint our preliminary observations [12] suggested that aluminum chloride paste deodorant preparations might reduce or abolish apocrine sweating. This early work has not been confirmed in our later more carefully controlled studies detailed below.

Methods: Ten healthy men were chosen for this study. These men had eccrine sweating of equal amounts in each axilla, as determined by the Randall starch paper-iodine technique. The axillae were shaved at the beginning of the study and on the sixth day. This was done in order to facilitate the proper prints with the starch paper-iodine method. Five-minute daily applications of 25% aqueous aluminum chloride solution were made in the one axilla for seven days. The opposite control axilla was similarly treated with plain water. At the end of this period simultaneous sweat imprints were made of both axillae. Satisfactory sweat responses could be obtained in the absence of any direct emotional or pharmacologic stimuli.

Fifty healthy men were selected from approximately 100 subjects for a study of apocrine sweat. All of these men had abundant and symmetrically equal apocrine sweat responses. The axillae were unshaved, and washing was limited to once daily. Nothing was applied other than the product under study. The following preparations were studied in 10 men each: (a) 25% aluminum chloride in aqueous solution; (b) spray deodorant A (commercial); (c) spray deodorant B (commercial); (d) cream deodorant (commercial); (e) zinc oxide paste.

In the case of the aluminum chloride solution the application technique consisted of placing gauze pledgets (4 by 4 in. [10 by 10 cm.]) saturated with the solution in the axilla for five minutes daily for seven days, as was done previously in these studies. All other test substances were applied in one axilla once a day for seven days. In all instances the opposite axilla served as a control and was untreated except for the usual washing. At the end of a week the

11. Sulzberger, M. B.; Zak, F. G., and Herrmann, F. J.: Studies of Sweating: II. On the Mechanisms of Action of Local Antiperspirants, Arch. Dermat. & Syph. **60**:404, 1949.

12. Shelley, W. B.: Apocrine Sweat, J. Invest. Dermat. **17**:255, 1951.

axillae were carefully cleansed with alcohol to remove all debris, accumulated cream, paste, or liquid deodorant, so that there would be no difficulty in identification of the apocrine sweat. These men were then given a standard test dose of epinephrine (0.15 cc. of 1:1000 solution) subcutaneously in each axilla. We then observed the amounts of apocrine sweat produced, and compared the control and test sites.

Results: In all 10 subjects no significant reduction in the amounts of eccrine sweating was noticed as shown by the prints with the Randall starch paper-iodine technique. Comparison of these prints on the seventh day with those taken before the experiments began revealed no appreciable change.

No significant decrease in the quantity of apocrine sweat could be detected on the treated or the untreated axillae. In three of the men who had used the aluminum chloride preparations miliaria vesicles were produced on the treated areas.

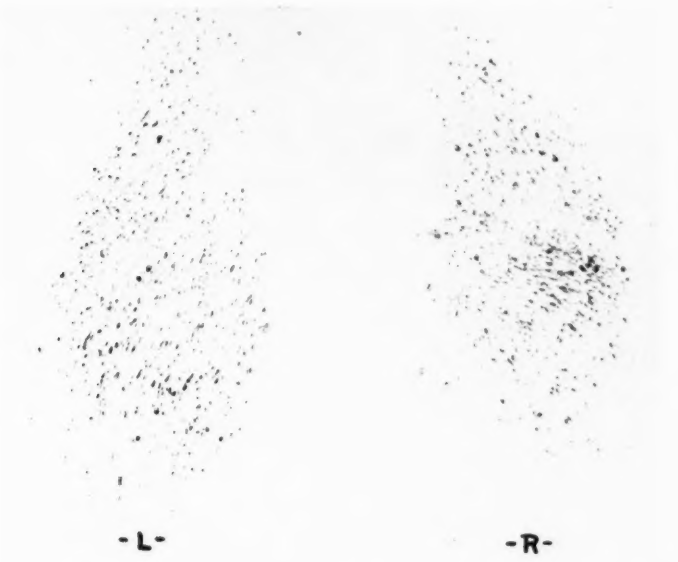

Fig. 5.—Axillary imprints made by the Randall starch paper-iodine method to detect eccrine sweating. Each black dot represents a droplet of eccrine sweat. These prints are from 1 of 10 subjects who had had daily five-minute applications of aluminum chloride to the right axilla and tap water to the left axilla for one week. The above imprints are representative of all that were taken. Note the absence of any difference on treated or control sides.

Comment: The lack of any significant reduction in axillary eccrine sweating following the application of aluminum chloride may seem paradoxical. Admittedly, on other nonflexural body sites, such as the back or abdomen, such treatment would definitely produce some degree of anhidrosis, which after repeated application of the aluminum salts would become more and more complete. However, a satisfactory explanation of this deviation may be that the axillary eccrine sweating constantly washes away the aluminum salts and thus prevents the usual effects of these substances elsewhere, viz., injury to the keratin with subsequent eccrine poral occlusion, and resultant anhidrosis. If this explanation is correct, it would be anticipated that

persons showing minimal sweating in the axillae would derive the greatest relative antiperspirant effect of these aluminum agents. None of the subjects studied by us fell into this hypohidrotic group.

Several vehicles were employed in the study of the effects of these preparations on apocrine sweating. Ointment and liquid commercial deodorants, which contain perfumes as well as aluminum salts, and a simple 25% aqueous aluminum chloride solution were used. All axillae were given maximal exposure to the test substances. The zinc oxide paste was employed to determine the possible mechanical blocking effect of such preparation. It, too, was ineffective in producing any reduction in apocrine sweating. This might be expected since these glands will secrete against an external pressure of 225 mm. of mercury.[2b]

Conclusions: By qualitative test methods no significant reduction in the amount of aprocrine or eccrine sweating could be demonstrated following the repeated use of aluminum chloride preparations.

B. Deodorant Activity of the Aluminum Salts.—Since it has been shown that the aluminum preparations as commonly used in the axilla do not possess appreciable antiperspirant activity, it would appear their chief role is that of a deodorant. Their continued use by so many persons obviously supports such an assumption. Studies were undertaken, therefore, to evaluate the magnitude and significance of this reputed action.

Method: The unshaved axillae of 10 healthy men were cleansed daily as usual. Saturated pledgets containing 25% aqueous aluminum chloride solution were applied daily for five minutes to one axilla for seven days. A similar application of water was used on the control axilla.

These men were then examined for axillary odor at 2 and 18 hours after the last application.

Results: At two hours, 6 of the 10 subjects showed absence of any axillary odor on the treated side. The remainder of these men showed an alteration of the typical axillary odor to a relatively inoffensive one. At 18 hours 2 of the 10 subjects showed abolition of the axillary odor on the treated side, and 2 showed alteration. The remaining six men had typical axillary odor. In all of the subjects the control axillae presented a pungent offensive odor.

Conclusion: Aluminum chloride preparations have deodorant activity. They may completely abolish axillary odor in some individuals for 12 to 18 hours or may render the usual axillary odor relatively inoffensive so that it will be disregarded.

C. Mechanism of Deodorant Action of Aluminum Salts.—The problem of mechanism of action of the deodorant preparations containing aluminum salts, was then explored. It was felt that the action might be antibacterial and/or chemical in nature. The following studies were done to investigate these possibilities.

Methods: Ten healthy men were again chosen for study. The axillae were unshaved and were cleansed daily as usual. On one axilla a saturated pledget of 25% aqueous aluminum chloride solution was applied daily for five minutes for three days. A similar application of water was used on the control axilla. Two and one-half hours after the last application, the men were examined, and axillary hairs were selected from the axillae and placed on blood agar plates. These hairs were collected with scissors and forceps which were kept sterile at all times. One hair was placed on each culture plate. The cultures were then incubated at 37.5 C. for 48 hours.

Pooled apocrine sweat was collected then from 20 normal healthy men and placed in a small vial. At the end of 48 hours a very strong odor developed in this vial. One-tenth cubic centi-

meter of this apocrine sweat was then added to 3 cc. of distilled water and to a 25% aqueous aluminum chloride solution, respectively. The specimens were then examined immediately for any odor change.

Results: Of the aluminum-chloride-treated axillary hairs from the 10 subjects, six showed no bacterial growth on the agar plates; four showed good growth. The axillary hairs of the control side all showed luxuriant bacterial growth at 48 hours. An example is illustrated in Figure 6.

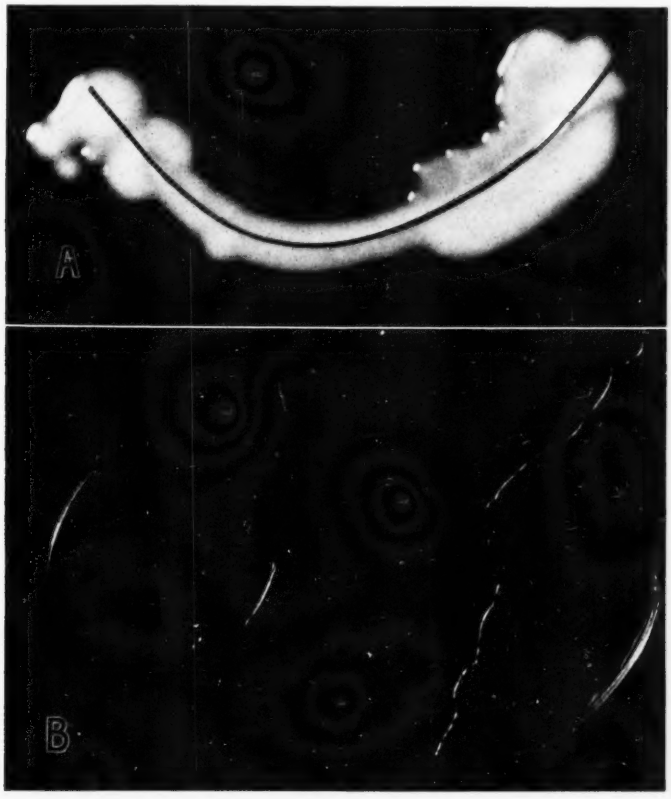

Fig. 6.—*A*, a hair which was taken from the axilla of a subject who had daily five-minute applications of tap water to one axilla for three days. Note the luxuriant bacterial growth on the agar plate after 48 hours' incubation at 37.5 C. *B*, a similar hair from the opposite aluminum chloride-treated axilla in which no such growth is present.

The specimen containing water plus apocrine sweat gave the typical acrid odor one might expect. However, an instantaneous odor change occurred in the solution containing the aluminum chloride and apocrine sweat. The resultant odor was decidedly different from the original odor and may be described as a somewhat sharp yet relatively inoffensive scent. Dilution of this solution of the apocrine sweat and aluminum chloride resulted in a gradual diminution of the odor to the point

where it became somewhat pleasant. This odor was similar to the altered odor noted in the axillae of the men treated with the aluminum chloride in the previous experiment.

Comment: Certain aluminum salts are antibacterial,[13] and the experiment above supports this fact. The effect is limited, however, and was not as marked as was seen in the hairs from the hexachlorophene-washed axilla.

It is probable, therefore, that much of the deodorant effect of aluminum salts is antibacterial in nature.

Conclusion: The deodorant action of aluminum chloride preparations is twofold in mechanism. There is both an antibacterial effect, thus preventing odor development, and a chemical change, thus rendering the normal odoriferous products of bacterial decomposition inoffensive.

GENERAL COMMENT

Although scientific section discussion has been given, some features of this study deserve further clarification and amplification.

In the normal person we have noticed some variation in the type of axillary odor produced in the absence of any special soap, deodorant, antiperspirant, or perfume. We have arbitrarily divided these odors into three general categories: (1) typical acrid body odor, which is commonest and which requires little description; (2) a rancid odor, which is quite intolerable and reminds one of rancid butter; (3) a relatively vague, indistinct, and less offensive odor.

In addition, there are occasional odors which are unique. It should be stressed that all of these odors are quite different from other body odors and would not in any way interfere with the identification as axillary odor. They are all easily distinguished from the odor of contaminated eccrine sweat, for example, or that of sebum, urine, or feces.

The axilla, as an intertriginous surface with maximal amounts of secretion and optimal growth conditions, is responsible for a large number of bacterial colonies. Little is written regarding the normal bacteriology of the axilla, and an attempt was made by us to outline the normal range of flora in the axillae of our subjects. Swabs taken from the axillae of 20 healthy men were inoculated on blood (horse) infusion agar, and, in general, the following bacteria were found routinely: (1) Micrococcus pyogenes, var. aureus (coagulase-positive Staphylococcus); (2) Micrococcus pyogenes, var. albus (coagulase-negative Staphylococcus); (3) Cornebacteria; (4) Aerobacter aerogenes; (5) Sarcina lutea.

Speculation upon the relative effects of the various bacteria is interesting. One might assume that the presence of the coliform organism would allow for a fecal odor of some sort. However, this does not seem to be the case. As a matter of fact, in two instances in which apocrine sweat was collected from the unsterile axilla of a normal healthy Negro such sweat developed a rather pleasant odor after about 48 to 72 hours. This odor remained pleasant even at the end of seven days. Bacteriologic

13. Meyer, E., and Vicher, E. E.: Germicidal Activity of Alcohol, Hydrochloric Acid and Aluminum Potassium Sulfate: Their Effect on Cutaneous Flora, Arch Surg. **47**:468, 1943.

examination of both specimens revealed pure cultures of Aerobacter aerogenes. This may indicate that individual variations in axillary odor may reflect either chemical differences in aprocrine sweat or differences in resident bacteriologic flora or both.

It is interesting to note that in a young white man suffering from severe axillary eccrine hyperhidrosis relatively little axillary odor was encountered, in spite of definite apocrine gland activity. It is likely that the enormous amounts of eccrine sweat produced continually washed away all apocrine secretion and thereby the substrate necessary for the production of axillary odor.

Comment should be made concerning the fact that the odor of the axilla arises in a manner common to odors of diverse nature, namely, on the basis of bacterial activity. Hence the apocrine gland cannot be viewed as a specific scent gland, and the bacterial genesis of axillary odors seriously imperils some of the teleological theorizing as to the sexual significance of axillary odor.[14]

Recently chlorophyll has received a great deal of publicity regarding its role as a deodorant. We are unable to attribute any specific axillary deodorant action to chlorophyll after oral administration. In five subjects who took daily 600 mg. oral doses of chlorophyll for seven days there was no odor reduction as compared with the initial axillary odor before administration of the drug. These findings support those of Brocklehurst.[15]

Finally, we may glean from this work some practical recommendations regarding the most effective means of reducing or inhibiting axillary odor. There is no uniformly effective way of significantly diminishing apocrine or eccrine sweating of the axilla. We are forced to rely almost completely, therefore, on a deodorization process. Clearly, the most complete and prolonged means of preventing axillary odor includes shaving of the axillary hair, plus the topical application of a potent antibacterial substance, such as hexachlorophene. We used pHisoHex because of its proved bacteriostatic[3] effect, ease of application, and low sensitizing index.

SUMMARY AND CONCLUSIONS

1. Apocrine sweat is odorless and sterile when it initially appears on the skin surface.

2. Axillary micro-organisms acting on the apocrine sweat in vitro will promote the development of the typical acrid axillary body odor within a few hours. Exclusion of these organisms (sterile apocrine sweat) or inhibition of their growth (addition of hexachlorophene to the sweat) will prevent any odor from developing.

3. The only substrate required for the production of this distinctive malodorous scent is apocrine sweat.

4. From a practical standpoint, the intensive use of hexachlorophene-detergent preparations will abolish the axillary odor for more than 18 hours in most persons.

5. The presence of hair greatly increases axillary odor, since it acts as a collecting site for axillary secretions, debris, keratin, and bacteria. Shaving and careful washing of the axilla eliminate odor for more than 24 hours.

14. Schiefferdecker.[1] Kuno, Y.: The Physiology of the Human Perspiration, London, J. & A. Churchill Ltd., 1934.

15. Brocklehurst, J. C.: Assessment of Chlorophyll as a Deodorant, Brit. M. J. **1**:541, 1953.

6. Pure eccrine sweat, whether sterile or unsterile, neither has nor develops an odor. Eccrine sweat, contaminated with sebum, keratin, or debris, develops odor presumably as a result of bacterial action. This odor is mild and very definitely distinct from the odor developing in pure apocrine sweat. The role of the eccrine sweat in the production of axillary odor consists of an accentuation of bacterial growth and also the volatilization of the odoriferous compounds derived from apocrine sweat.

7. No significant reduction in eccrine or apocrine sweating was seen following the use of preparations containing aluminum salts.

8. Aluminum preparations have demonstrable deodorant activity. Daily applications of these substances will abolish or alter the usual axillary odor in many persons for 12 to 18 hours.

9. This deodorant activity in the case of aluminum chloride is based on antibacterial action and a chemical effect on the odoriferous products.

Society Transactions

BRONX DERMATOLOGICAL SOCIETY

Rudolf L. Baer, M.D., *President*

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Feb. 19, 1953

Lymphocytic Infiltration of the Skin. Presented by Dr. Max Jessner and Dr. Norman B. Kanof (Kodachrome presentation).

Lymphocytic Infiltration of the Skin. Presented by Dr. Abraham J. Orfuss.

W. R. T., a man aged 40, first noticed the condition in June, 1945. At present there is an erythematous papulation on the right zygomatic area and to a lesser extent on the left. These areas vary in size, are sharply defined, discrete, and fade when pressure is applied. Some telangiectasis and patulous follicles are observed. Scaling has never been present. No lesions are observed elsewhere on the body.

Physical examination was negative. Urinalyses were repeatedly negative and normal, as were the complete blood cell counts, sedimentation rates, blood chemistries, liver function tests, blood serologies, prostatic smears, x-ray studies of the heart and lungs, and electrocardiograms.

Histologic examination performed in 1947 by Dr. Arthur Allen at the Army Institute of Pathology revealed changes indicative of discoid lupus erythematosus, with acute exacerbation. Histologic examination on Jan. 26, 1953, by Dr. L. C. Rubin revealed a thinned epidermis, with loss of rete pegs. There was some hyperkeratotic follicular plugging but no diffuse hyperkeratosis. The basal cell layer and the skin appendages were intact. The cutis, especially in the upper half, was rather edematous. A diffuse and focal infiltrate occupied most of the cutis, especially the upper half; but nowhere did it reach the epidermis, beneath which was a narrow zone without any infiltrate. The infiltrate was composed almost entirely of small round cells, with round, deeply staining nuclei. Intermingled with these cells were a few reticulocytes and plasma cells. There were no germinal centers and no mytotic figures. The infiltrate tended to surround the small blood vessels whose walls were edematous. There were no telangiectatic vessels. The upper cutis showed moderately severe basophilic degeneration. The histologic diagnosis lies between lymphocytoma cutis and lupus erythematosus, with the balance of evidence in favor of lymphocytoma cutis.

Treatment to date has consisted of injections of bismuth subsalicylate, one x-ray treatment (with severe exacerbation), sun screening preparations, nicotinamide administered orally, tocopherol (vitamin E), phenindamine (Thephorin), paraaminobenzoic acid, penicillin, chlortetracycline (aureomycin), carbon dioxide administered locally, quinacrine (Atabrine) dihydrochloride (its use had to be discontinued because of severe diarrhea), and psychotherapy.

DISCUSSION

Dr. Max Jessner: Dr. Kanof and I presented a group of cases, the nature of which I began to recognize about 10 years ago. We summarize the clinical picture, course, diagnosis, and histology as follows: The lesions are flat, discoid, more or less elevated, pinkish to reddish brown, starting as small papules, expanding peripherally, sometimes clearing in the center, sometimes showing a circinate arrangement. The surface is smooth, occasionally uneven. There is no follicular hyperkeratosis. The consistency is firm. There may be only one, a few, or numerous lesions. They persist for weeks or months or longer, disappear without sequelae, and may recur in the same or other areas and cause practically no subjective symptoms. The face is obviously the area of predilection, but other parts of the body may or may not be affected. These cases must be distinguished particularly from cases of chronic discoid lupus erythematosus, under which label they are invariably described; also from sarcoid, tuberoserpiginous syphilid, and drug eruption.

There are no enlarged lymph nodes. The blood cell count shows only an occasional relative lymphocytosis. The bone marrow smear reveals no abnormalities.

Histologically, the findings are rather constant. The epidermis may be stretched but is otherwise uninvolved. There may be edema in the subpapillary region in fresh lesions; older ones show none. Distributed through the cutis are rather sharply circumscribed lymphocytic infiltrations, sometimes extending to the subcutaneous fat, frequently, but not always, around vessels and/or appendages. The infiltrates consist of lymphocytes, mostly small ones, and usually a few histiocytes and plasma cells. The infiltrates are often enmeshed in a fine reticulum. There are no eosinophiles, no germinal centers or germinal center-like formations.

The evaluation of therapy in a condition so prone to spontaneous remission is extremely difficult, but speedy resolution has been noted following the administration of penicillin, bismuth, arsenic, sulfapyridine, quinacrine dihydrochloride, paraaminosalicylic acid, x-ray therapy, and Staphylococcus ambotoxoid.

We reviewed the pertinent European and American literature to separate this group from *(a)* the "true lymphocytomas as described in 1935 by Stephan Epstein, from the Breslau University Hospital, and more recently by Loveman and Fliegelman and Mopper and Rogin; *(b)* the "reticuloses" of the French literature, named by Werner Jadassohn, and *(c)* the Spiegler-Fendt sarcoid and lymphoblastoma.

Dr. Norman B. Kanof: Despite the work done on these cases, there is still a great deal we do not know, and it would be profitable to hear the views of those who have observed these cases.

Dr. Abraham J. Orfuss: I am grateful to Dr. Jessner for clarifying this symptom complex. I have been following five or six such cases since 1946. I can now recognize them clinically, but I do not know into what category to place them. Are they the seborrhea congestive form of lupus erythematosus? Are they fixed drug eruptions or erythema multiforme? These are usually the histopathologic reports given by the dermatopathologist. I do not know the incidence of the disease in the sexes, but I do not recall observing a single case in a female patient. Also the only locations for the lesions in my cases have been the zygomatic areas, the sides of the neck or the back, with one patient showing a striking zosteriform distribution of the lesions of the back. Contrary to Dr. Jessner's experience, the one patient treated with x-ray had a severe exacerbation following the treatment. These cases seem to respond to treatment irregularly and seem to have spontaneous remissions and exacerbations.

Dr. Stanley Kimmelman (by invitation): I would like to report eight cases of lymphocytic infiltration of the skin observed in Dr. Rein's office. Of the eight cases, seven were diagnosed as lymphocytic infiltration of the skin when first observed. The other case was diagnosed as lupus erythematosus. Biopsy specimens were taken in all eight cases and were reported as lymphocytic infiltration by Dr. Jessner. Three of these patients were treated with penicillin and Staphylococcus ambotoxoid. Two showed complete remissions, and the other was markedly improved. Three were treated with atabrine dihydrochloride, and the condition was healed completely in all. The time necessary for healing was from two to six weeks. One of the above-mentioned patients was a Japanese girl, treated with penicillin and Staphylococcus ambotoxoid, who showed a remission in two weeks but since then has had repeated exacerbations, each responding promptly to penicillin. Another of these patients was a woman from Florida who also was treated with penicillin and Staphylococcus ambotoxoid, responding moderately well. She returned to Florida with instructions to her physician to continue the treatment. Later oxytetracycline (Terramycin) was substituted, with some response. A few months later, she returned to Dr. Rein's office after an exacerbation and was given quinacrine dihydrochloride, showing 90% improvement in one week. She returned to Florida and has since shown complete remission on the administration of this therapy.

Dr. Paul Gross: First, I wish to congratulate Dr. Jessner on his most clarifying presentation. I was somewhat startled by his mentioning lymphocytoma as a possible diagnosis in these cases, and I am glad that he completely ruled out any relationship to this condition.

I believe that Dr. Jessner has given a clear histologic demonstration of this unique lymphocytic infiltration. Nevertheless, from my observation in such cases, what appears clinically as infiltration is partly due to edema. This fact, the evolution of the lesions, characteristic distribution, and the tendency toward spontaneous involution suggest some relationship to the

erythema group. Of course, the individual lesions persist much longer than those of erythema multiforme, but the persistence of the lesions could be compared with that of the erythema annulare centrifugum of Darier. I accept the fact that this is a clinical entity; but on the basis of the clinical picture, I am inclined to consider it a hyperallergic reaction. The temporary response in some of these cases to broad spectrum antibiotics, like chlortetracycline (aureomycin), remind me of a possible infectious allergy.

DR. SAMUEL B. FRANK: I have observed nine such cases in my private practice. All the patients were adults; only one was a woman. I have not found any type of therapy particularly efficacious in managing this problem. I plan to restudy the biopsy specimens I have for the findings that Dr. Jessner has described. I want to compliment Dr. Jessner for his presentation of this entity.

DR. ALEXANDER A. FISHER: Is there a clear-cut clinical distinction between this entity and eosinophilic granuloma?

DR. HERMAN BEERMAN (by invitation): Many of the features of lymphocytic infiltration resemble lupus erythematosus, particularly the epithelial changes and the edema; but the infiltration is much deeper. In a forthcoming paper, Cohn, Levy, Shaffer, and I describe a patient's abnormal reaction to light (the patient was accidentally overexposed to light). The reaction was severe, and the histologic picture indicated lupus erythematosus. Since then we have been studying a number of these cases, and, perhaps, they really represent lymphocytic infiltration of the skin.

DR. CHARLES R. REIN: Dr. Jessner is to be highly commended for his most interesting, timely, and worthwhile presentation. I am especially grateful to him for calling this condition to my attention and for teaching me how to recognize it. As previously stated by Dr. Kimmelman, we have observed eight patients with this condition, and I am certain that most dermatologists have also observed such patients. Unfortunately, many of these cases are diagnosed as lupus erythematosus and given needless and sometimes disfiguring therapeutic regimens. One patient in our series received numerous scars from carbon dioxide therapy.

DR. MAX JESSNER: I thank the discussers for their friendly and kind words. In answer to Dr. Orfuss, I do not, as yet, know enough about sex distribution in these cases. In answer to Dr. Gross, I do not believe that the cases belong in the group of erythema annulare. From a practical point of view, it is most important that these cases be properly grouped and not treated with all kinds of possible dangerous drugs. With regard to Dr. Fisher's question about eosinophilic granuloma, they are "granulomas" that usually show larger numbers of eosinophiles, and that is all we know. But these surely do not belong to our group.

Herpes Gestationis (Rh-Positive, Type O) Treated with Cortisone and Progesterone. Presented by DR. ALEXANDER A. FISHER.

M. B., a woman aged 25, is a secundigravida. In November, 1951, in the fifth month of her first pregnancy, a severely pruritic, papular eruption appeared, which became progressively worse as the pregnancy advanced. Immediately after delivery, the eruption cleared and she was well for two days. On the third day post partum, her temperature rose due to an unknown cause, for which she received penicillin. In the fourth day post partum, a bullous eruption appeared which persisted for two weeks and required an unknown amount of cortisone. The patient remained well until December, 1952, when in the second month of her second pregnancy, there again appeared an intensely pruritic bullous eruption.

When first observed on Jan. 26, 1953, she presented a generalized bullous eruption with marked involvement of the trunk and extremities. The face, scalp, and mucous membranes were free of lesions. Bullae arose from a faintly erythematous base and varied from the size of a split pea to that of a cherry. There was no grouping of the lesions. The patient had been unable to sleep since the onset of the eruption. A physical examination gave findings within normal limits. She was given 50 mg. of progesterone daily (as suggested by Keaty and others) for 10 days but new lesions continued to appear, and the itching continued to be severe.

On Jan. 30, 1953, she was given 200 mg. of cortisone daily for two days and 100 mg. of cortisone for five days. Within two days no new bullae appeared, and within four days all the bullae had dried. It was then found that the eruption could be controlled with a daily administration of 50 mg. of cortisone and 100 mg. of progesterone.

DISCUSSION

DR. FRANK E. CROSS: Usually this condition is difficult to treat, and the results so far obtained appear encouraging. These patients are uncomfortable throughout gestation and often after childbirth.

DR. HANS H. BIBERSTEIN: Can anyone enlighten me regarding the effect of cortisone, given at any time during pregnancy, on the fetus and the infant after birth? It is known that herpes gestationis responds well to treatment with arsenic, without any damage to the fetus; therefore, I would prefer the use of arsenic, unless there is sufficient evidence from practical experience with cortisone in these cases to indicate its use without harm to the fetus.

DR. MAX B. KAMPF: Some years ago I presented before the Society a case of herpes gestationis in which the eruption did not appear until the fifth month of pregnancy and was not severe enough to cause discomfort until the seventh or eighth month. A corpus luteum preparation was administered, with considerable relief of her symptoms. However, the eruption persisted in a mild degree until after she was delivered of the baby, and then it cleared completely.

DR. JOHN GARB: In 1945, I experimentally treated a patient suffering from herpes gestationis with nicotinic acid (Niacin). Johnson and Binkley (Nicotinic Acid Therapy of Dermatitis Herpetiformis, *J. Invest. Dermat.* **14**:233 [April] 1950) report a similar beneficial effect with nicotinic acid (50 to 200 mg. four times a day) in 6 out of 12 patients suffering from dermatitis herpetiformis. Roniacol (an ethylated derivative of nicotinic acid) tartrate was used with equally good results by Philpott and his associates (Roniacol Tartrate in the Treatment of Dermatitis Herpetiformis, *J. Invest. Dermat.* **18**:87 [February] 1952). The effect of nicotinic acid and its derivative Roniacol tartrate appears to be due to the pressure of the pyridine radical. It would be safer therefore to attempt to use a drug such as nicotinic acid before using cortisone, which may have untoward effects on the fetus.

DR. ALEXANDER A. FISHER: An interesting fact is that the patient is Rh-positive, type O. This has been brought to our attention only recently by Edward P. Cawley, Clayton E. Wheeler, and Philip A. Wilhite ("Herpes Gestationis and the Rh Factor," *South. M. J.* **45**:827 [Sept.] 1952). Obviously, with an Rh-positive patient, isosensitization by the Rh factor is not a possibility in the production of herpes gestationis. When erythroblastosis of the fetus or herpes gestationis occurs in Rh-positive mothers, it is felt that isosensitization may be induced by the A or B factors. However, this explanation does not hold in my patient because she is type O. We must therefore conclude that in this particular case of herpes gestationis, isosensitization does not play a role.

With regard to the use of arsenic, I can state that solution of potassium arsenite (Fowler's solution) failed to produce satisfactory results. As to Dr. Garb's suggestion concerning the use of nicotinic acid, I have under my care another patient with herpes gestationis who is not responding to nicotinic acid.

As to the dangers of the use of cortisone during pregnancy, it would seem that preliminary reports show that it is rather safe for the mother and fetus (E. J. DeCosta and M. A. Abelman: Cortisone and Pregnancy: An Experimental and Clinical Study of the Effects of Cortisone on Gestation, *Am. J. Obst. & Gynec.* **64**:746 [Oct.] 1952).

In a personal communication, Dr. Maurice J. Reutar, of Milwaukee, states the following: "Regarding my patient whom I have treated through five pregnancies with herpes gestationis, there has been no untoward effect on either the mother or the child as a result of therapy with cortisone or corticotropin (ACTH)." The literature up to date also supports the fact that if the above hormones are indicated during pregnancy, adverse effects on the fetus have not been observed. The reason for my initiating hormonal therapy was due to the patient's lack of response to sulfapyridine, which was rather efficacious in controlling the eruption during the patient's first two pregnancies.

As to the use of corticotropin as a substitute for cortisone, it seems to me that its action would be the same in herpes gestationis.

Dr. A. Rostenberg Jr., of Chicago, recently wrote to me that corticotropin in a dose of 20 mg. daily did not seem to produce any adverse effect during pregnancy. He also states that in Rh-negative mothers large doses have been used in the last part of the pregnancy with no apparent adverse effects.

NOTE.—Recently cortisone was withheld from this patient. There was a prompt recurrence of many blisters over the body accompanied by severe itching. Without progesterone, larger doses of cortisone apparently are necessary. The dose necessary for maintenance at present seems to be 50 mg. of cortisone and 100 mg. of progesterone daily.

Pemphigus. Presented by DR. LOUIS CHARGIN.

A Case for Diagnosis: Squamous Cell Epithelioma and Actinomycosis? Presented by DR. DAVID BLOOM and DR. JOSÉ HENRIQUES (by invitation).

Scleredema Adultorum (Buschke), Recurrent. Presented by DR. DAVID BLOOM.

Discoid Lupus Erythematosus with Extensive Scarring: Treated with Podophyllin. Presented by DR. JOHN GARB.

Rudolph L. Baer, M.D., *President*

Henry Silver, M.D., *Secretary*

April 16, 1953

The Present Status of Hydrocortisone Acetate Ointment in Dermatologic Therapy.

DR. MARION B. SULZBERGER.

Soon after their introduction into medicine, it became evident that corticotropin (ACTH) and cortisone had definite beneficial effects upon a very great variety of dermatoses, and it was also evident that the potential ill effects of these hormones were in many cases prohibitive.

It was therefore logical that one should attempt to see whether any method could be devised to reduce or obviate the ill effects while preserving the benefits. One of the first of these methods was the attempt to use cortisone locally upon the skin lesions concerned. Despite early favorable reports these efforts proved generally ineffective—with the possible exception of dermatoses on the eyelids and at or near the transitional mucous membranes.

A next logical step was to try local applications of hydrocortisone in place of local cortisone, particularly in view of the fact that it was shown that the hydrocortisone was locally much more effective when injected into arthritic joints than was cortisone applied in the same fashion. The topical applications of hydrocortisone in dermatology, as carried out for over a year by Dr. Witten, Dr. Smith, and me, have proved very encouraging indeed. We have already reported on the effects of topical applications of hydrocortisone acetate ointment in a series of patients with different disorders of the skin (*J. Invest. Dermat.* **19**:101-102 [Aug.] 1952, and *J.A.M.A.* **151**:468-472 [Feb.] 1953).

The Chart shows our results with 100 consecutive cases of selected dermatoses in which there was treatment with local applications of hydrocortisone acetate or hydrocortisone-free alcohol, in ointment form. Parenthetically, it may be mentioned that we have found no substantial differences between the effects of the free alcohol and the effects of the hydrocortisone acetate.

While these results are of course very promising and gratifying, numerous problems still remain, some of which are of great practical importance and others of which are of a very fundamental nature. Among these are the following: (1) Why do not all the skin diseases which are benefited by cortisone systemically respond to hydrocortisone locally? (2) Why do not all patients with a given skin disease respond equally well to the local applications of hydrocortisone? (It will be seen that about 75% of the patients with dermatoses in the groups benefited by local hydrocortisone respond well, whereas the remaining 25% of the patients are not helped.)

Another fundamental question which remains is: What is the mechanism of action of the locally applied hydrocortisone, and why does it act so much better when applied locally than does cortisone itself? Here it seems possible that the effective steroid is not cortisone itself but a derivative of cortisone which is formed in the body when cortisone is administered systemically (but which is not formed locally when cortisone is applied to the skin lesions). It appears quite possible that this active derivative may be hydrocortisone, and that this steroid is the actual effective local agent even when cortisone is given by the systemic route.

Still another basic series of questions relates to the possibility that the local effects of adrenocortical steroids may be the agency concerned when, as so often, skin lesions respond

to fever, autohemotherapy, shocks, "nonspecific" proteins, psychotherapy, "suggestion," etc. (Cerebral cortex → hypothalamus → anterior pituitary → adrenal cortex; i. e., the "cortico-cortical-axis.")

The Present Status of Hydrocortisone Acetate Ointment in Dermatologic Therapy.
DR. CHARLES R. REIN.

Since December, 1952, we have treated a series of 131 patients, selected from private practice, with a variety of dermatoses, including the following:

EFFECTS OF HYDROCORTISONE OINTMENT IN SELECTED DERMATOSES

DIAGNOSIS	# of Cases	Improved				No Change	Worse
		90 to 100%	75 to 90%	25 to 75%	0 to 25%		
Atopic Dermatitis	45	2	23	9	2	5	4
Pruritus Ani & Vulvae	6		2	2			2
Psoriasis	5					5	
Chronic Discoid Lupus Erythematosus	5				1	4	
Lichen Chronicus Simplex	4		2	2			
Pemphigus Vulgaris	2					2	
Alopecia Areata	3					3	
Discoid & Lichenoid Chronic Dermatosis	4	1		2		1	
Nummular Eczema	6		2	3		1	
Chronic Lichenified Dermatitis of Eyelids	3		2			1	
Chronic Contact Dermatitis	9		4	4	1		
Chronic Hand Eczema	3			1	1		1
Seborrheic Dermatitis	4			2	1	1	
Otitis Externa	1		1				
TOTAL	100	3	36	25	6	23	7

In most instances, cases were chosen in which the dermatitis involved symmetrical areas so that a comparison could be made with the ointment containing hydrocortisone acetate and the ointment base alone. In other cases, an attempt was made to evaluate the efficacy of various concentrations of hydrocortisone acetate (1.0%, 1.5%, and 2.5%). In another group, an attempt was made to compare the efficacy of the free alcohol with the acetate preparation in equivalent strengths.

In those patients in whom there was a marked improvement after the local use of the ointment the ointment base alone was used for an equal period, and differences in the therapeutic effect were noted.

Patients were supplied with the material and were receiving therapy for periods varying from one to three months. The following are the results obtained:

Atopic dermatitis. In our series of 41 patients, 14 showed a marked improvement, 7 a moderate improvement, and 9 mild improvement.

Anogenital pruritus. Of 21 patients, 9 were markedly improved, 4 were moderately improved, and 2 were mildly improved.

Lichen chronicus simplex. Of 18 patients, 11 showed a marked improvement, 4 a moderate improvement, and 1 a mild improvement.

Dermatitis venenata. Of 18 patients, 6 were markedly improved, 4 were moderately improved, and 4 were mildly improved.

Nummular eczema. Of 13 patients, 7 were markedly improved, 2 were moderately improved, and 1 showed mild improvement.

Intertriginous seborrheic dermatitis. Of seven patients, five were markedly improved and one was moderately improved, while one showed no improvement.

In the miscellaneous groups consisting of psoriasis, lichen planus, lupus erythematosus, alopecia totalis, mycosis fungoides, vitiligo, and parapsoriasis en plaques there was no objective improvement, but there was a diminution of the pruritus in the patients with lichen planus.

The 2.5% ointments appeared to be more effective than the 1% ointments, but the differences in efficacy were not proportionate to the increase in concentrations. In many instances, the 1% ointments gave satisfactory therapeutic results.

Although our experience with the free alcohol preparation has not been as extensive as with the acetate, it is our impression that they have equal efficacy.

There were four patients in whom there was a flare-up of the dermatitis after the use of the hydrocortisone acetate (Compound F) ointment. These patients were given patch tests with the free alcohol, the acetate, and the base, and in all instances negative reactions were obtained.

Two patients, one with mycosis fungoides and one with parapsoriasis en plaque, were treated with injections of 0.1 cc. to 0.2 cc. of 2.5% hydrocortisone in saline suspension. This material

Dermatosis		No. of Patients
Atopic dermatitis		41
Anogenital pruritus		21
Lichen chronicus simplex		18
Dermatitis venenata		18
Nummular eczema		13
Intertriginous seborrheic dermatitis		7
Miscellaneous		13
Psoriasis	5	
Lichen planus	3	
Lupus erythematosus, discoid	1	
Alopecia totalis	1	
Mycosis fungoides	1	
Vitiligo	1	
Parapsoriasis en plaque	1	
Total		131

was injected intradermally into the center of the lesions. Within one week after injection, both patients showed a 2 cm. halo of normal-appearing skin around a 1 cm. yellowish plaque. We suspect that the plaque consisted of unabsorbed hydrocortisone crystals.

CONCLUSIONS

1. Hydrocortisone ointments are a valuable adjunct in the treatment of atopic dermatitis, lichen chronicus simplex, anogenital pruritus, dermatitis venenata, and nummular eczema.

2. It was our impression that the 2.5% concentrations were more effective than the 1% ointments, but the differences in efficacy were not proportionate to the increase in concentration.

3. The free alcohol preparations and the acetate ointments appear to be of equal therapeutic value.

DISCUSSION

DR. ALEXANDER A. FISHER: Have the presenters had any experience with the use of this drug in inflammatory lesions of the mouth, applied topically, and what were the results?

DR. FRANK E. CROSS: Have these patients received therapy other than cortisone simultaneously?

DR. VICTOR H. WITTEN: From a practical point of view, because of the expense of the commercially available 2.5% hydrocortisone acetate ointment, we have added Aquaphor (an oxycholesterol-petrolatum ointment base) and thus diluted the concentrations to 1%; in this form it is a little softer and, in some cases, less irritating. We have also used the crystalline

suspension in saline which we have incorporated in Aquaphor, also making a 1% ointment. In the study of infantile eczema we have found it successful and better tolerated by the infant skin. In many instances this type of base is also better tolerated on the scrotum and the eyelids.

DR. PAUL GROSS: Dr. Sulzberger and Dr. Rein have presented the subject without undue enthusiasm. I am convinced that further clinical trials will prove hydrocortisone (Hydrocortone) acetate ointment to be one of the most important additions to dermatologic therapy. The results in atopic dermatitis are excellent, and I believe that by suppressing the vicious cycle of itching, rubbing, and lichenification with hydrocortisone ointment one is able to bring about complete reversal, at least in some of the mild and more localized cases. The value of the psychologic effect on the patient of having a remedy so effective, simple, and clean which will check promptly a flare-up of the dermatitis should not be underestimated. I also subscribe to the effectiveness of hydrocortisone ointment in pruritus ani and vulvae and in the lichenified cases of otitis externa.

DR. NATHAN SOBEL: I should like to bring out a minor point. In an extensive eruption of atopic dermatitis, one does not apply the ointment on all the areas but in thin amounts to the areas most inflamed, and here too one obtains gratifying results.

DR. JOSEPH SILVERBERG (by invitation): In a patient under my care, suffering from an eczema of the hand, one of the agents used was hydrocortisone acetate ointment. It was applied in the afternoon and once before bedtime. Several hours later there occurred an acute flare-up. Patch tests with the hydrocortisone acetate ointment gave a 2,3+ reaction. Several days later she was given a patch test with the Merck & Company, Inc., preparation of hydrocortisone and the compound suspected and again a 2+ positive reaction to both resulted. Then I gave her a patch test with all the constituents of the base manufactured by Merck & Company, Inc., except propylene glycol and obtained negative results. A patch test with straight cortisone gave a negative result.

DR. WILLIAM LEIFER: In otitis externa how was the canal portion treated? Was it treated with ointment or with some other form of the drug?

DR. HENRY SILVER: I am pleased that the presenters were somewhat modest in evaluating their results. In my experience, there was dramatic response in some cases. The question is what to do with diseases that keep on recurring, like nummular eczema. How long can one continue with this ointment?

The difference in the action of cortisone and hydrocortisone, when applied topically, throws some light on the therapeutic mechanism.

DR. CHARLES WOLF: I used this preparation in about 20 cases, and the results were excellent. After a short while, however, there was a relapse to the original state. I have not had a single case in which the good result was sustained. I believe that this drug has no permanency in clearing up inflammatory processes. Have the presenters seen any permanency in their results?

DR. PAUL GROSS: I have seen three cases of hypersensitivity to the ointment but cannot tell as yet whether it was an allergic reaction to the drug itself, or to the polyethylene glycol (Carbowax) base, or whether it was due to physiologic effect on the specific eczematous eruption unrelated to allergy.

DR. RUDOLF L. BAER: My own experience with hydrocortisone acetate ointment is similar to that of the previous speakers. I also agree that psoriasis on the glabrous skin and scalp does not respond to hydrocortisone ointment, but I believe that some cases of psoriasis of the vulvar and perianal area are benefited, as are some cases of other eruptions and pruritus in the vulvar and anal areas. Regarding otitis externa, in a few cases Dr. Litt and I have used a combination of hydrocortisone ear drops and ear drops containing polymyxin B. The results thus far seem to be encouraging.

Most cases of otitis externa probably start out as psoriasis or seborrheic dermatitis or eczema in the ear canal, with secondary infection supervening. The combination of the anti-inflammatory action of hydrocortisone and the antibiotic activity of polymyxin, especially against Pseudomonas aeruginosa, appears to be a logical approach in these cases.

DR. FREDERICK REIS: At the Manhattan Eye and Ear Hospital, a procedure which we follow at the clinic in otitis externa is to administer cortisone orally. With cortisone treatment

we give a local application of 1% iodochlorhydroxyquin (Vioform) or polymyxin B-bacitracin ointment (Polysporin) ointment. The patients were followed up, and all remained without symptoms. It is essential to give small doses of cortisone, and in such instances no flare-up or increase of infection should be expected.

Dr. Marion B. Sulzberger: Although Dr. Rein and I worked independently it is both striking and gratifying to note the close similarities in our results and in the percentage of benefits achieved with local hydrocortisone in various dermatoses.

In reply to Dr. Fisher, we have had no experience with topical hydrocortisone in ordinary inflammatory lesions of the mucous membranes other than of the eye. We did try it in persistent oral lesions of pemphigus vulgaris, without benefit; but then, its application did not benefit the cutaneous lesions of pemphigus vulgaris either. In answer to Dr. Cross—yes, we did often treat the patient with other remedies also, but these were usually the remedies previously ineffective, which were simply continued. Moreover, in almost every instance we compared the hydrocortisone ointment with a control blank ointment applied to symmetrically situated sites. Moreover, in many cases, without changing any other treatment, we alternated the periods of use of hydrocortisone ointment with periods of using the vehicle alone and could observe the improvements and exacerbations of the dermatosis, synchronous with the use of hydrocortisone ointment and the placebo ointment.

Dr. Witten has brought up the matter of the vehicles, or ointment bases. We have used four or five different kinds. The present purchasable base (with zinic stearate, propylene glycol, polyethylene glycols) is excellent for many purposes, but it is also likely to be too drying for many other purposes, for instance, on the hands during the winter. It is certain that several different kinds of vehicles will be necessary in order to achieve a wide spectrum of usefulness, and this applies also to different concentrations of the hydrocortisone in the vehicles. We are just now working on both these problems, each of which requires long clinical studies. This material is not likely to prove valuable unless it reduces the dangers of systemic effects because of its low rate of absorption. We too feel that this is the heart of the matter, and that all our evidence indicates that the systemic absorption is negligible under the conditions of use. In well over 200 patients for about 14 months we have never seen the slightest suspicion of a systemic effect from topical hydrocortisone. Moreover, in experiments which C. C. Smith of our group is now publishing, no fall of circulating eosinophiles has been produced by deliberate repeated inunctions of hydrocortisone acetate ointment into large areas of normal skin or into large areas of damaged skin (atopic dermatitis, exfoliative dermatitis, etc.).

As far as cure is concerned, here I believe that the situation is similar to that with cortisone used systemically. The effect of topical hydrocortisone is morbid, not curative. However, experience with cortisone used systemically indicates that many chronic diseases seem to be able to cure themselves if the cortisone is administered over long periods (years), with gradually diminishing doses. And we have reason to believe that a similar or even more optimistic outlook is justified in regard to local hydrocortisone, which can probably be continued with impunity for as long a period as necessary.

As to Dr. Gross's and Dr. Muskatblit's questions regarding otitis externa or anogenital pruritus possibly due to fungous infections—while both cortisone by mouth and local hydrocortisone ointment work well in many cases, this does not necessarily deny the roles of Ps. aeruginosa, of Candida or of other fungi and micro-organisms. Perhaps the change of soil, of terrain, the reduction of inflammation, scaling, oozing, itching, etc., which systemic cortisone or local hydrocortisone brings about may make the site less favorable for the growth and activities of the invading micro-organisms. Thus, there may be infections which are caused to spread and flare by cortisone or hydrocortisone (e. g. tuberculosis, peritonitis) and others which may be counteracted or inhibited by the same hormones. Here is one of the large promising fields for future studies.

As I have emphasized to the drug manufacturers, and as has again been rightly emphasized by Dr. Sobel and several other discussers this evening, the high price and small tubes of the present hydrocortisone ointment are serious limiting factors to its use in extensive and/or chronic dermatoses. If tar or mercury or sulfur ointment came only in such minute packages at such a cost, I believe that they would soon be judged to be relatively ineffective or unpractical in most skin diseases. However, the problems of price and quantities available as well as of various

concentrations and vehicles are now under attack, and I have no doubt that with time the material will be available in larger amounts, at lower prices, and in a flexible assortment of vehicles.

DR. CHARLES R. REIN: Dr. Sulzberger has so aptly answered all questions that were brought up that it will not be necessary for me to repeat. I am in full accord with Dr. Sulzberger's comments. Some patients with persistent pruritic dermatoses of many years' duration (especially pruritus ani) obtained relief within 48 hours after using hydrocortisone ointment, and when the medication is discontinued several days later, there may be no recurrence of the pruritus. In other dermatoses, there may be a recurrence within a few days or weeks after the medication has been discontinued, so that it becomes necessary to resume this form of therapy. In others, it is often possible to maintain relief of symptoms by use of the older forms of therapy after the original prompt response to hydrocortisone acetate (Compound F) ointments.

CHICAGO DERMATOLOGICAL SOCIETY

James R. Webster, M.D., *President*

Irene Neuhauser, M.D., *Secretary*

Jan. 21, 1953

Lupus Vulgaris. Presented by DR. STANLEY HUFF.

DISCUSSION

DR. H. E. MICHELSON, Minneapolis: Papulonecrotic tuberculid is not common. In fact, it is an extremely rare disease, and I believe one gets a false impression, because the same patients are seen over and over again. Even in Berlin, from whence a recent report tabulated some 500 cases of tuberculosis of the skin treated, there were only 3 cases of necrotic papular tuberculid. In the patients shown, I was inclined to disagree with the diagnosis, because the lesions were not distinctly hard papules with central necrosis, and the microscopic section did not show the tuberculoid structure that one almost must find to verify the diagnosis.

DR. ADOLPH ROSTENBERG: I should like to make a few comments about the first case. One might raise two general questions: What is the diagnosis in this case, and what are papulonecrotic tuberculids? I think Dr. Michelson has adequately covered the question of the diagnosis. I do not think there is much evidence for calling it a chronic papulonecrotic tuberculid. I would now like to raise a few questions as to what are papulonecrotic tuberculids. I think the whole concept of tuberculids, the legitimacy for labelling a particular clinical entity as one, demands reexamination. Much of the work on which these concepts are based is very old. There have been many new developments in technique which could be applied for a reexamination of many of these questions. Papulonecrotic tuberculids are supposed to develop because of embolic material lodging in a small vessel, and then in the allergically hypersensitive patient the lesion follows. I have never seen any proof of that. I am skeptical that a few tubercle bacilli lodging in a vessel could produce such a reaction. I do not think, because the histology resembles tuberculosis, that it has any special weight as to the diagnosis. Dr. Harris and I, at the University of Illinois, are about to try the Moro reaction, i. e., testing across the lesion with a tuberculin ointment. The theory is that the lesion itself should be more sensitive than the surrounding pattern. One would have to use a control to make sure the lesion was not hyperreactive to anything rubbed over it. I think if one could show a specificity, one would have a better basis for diagnosis.

DR. STEPHEN ROTHMAN: I agree with Dr. Rostenberg that it would be desirable to know more about the pathomechanism of tuberculids. But I think it is going a little too far to say that there is no evidence whatsoever for tuberculids arising from hematogenous showers and subsequent embolizations in the sensitized organisms. In his early experiments Lewandowsky showed that tuberculids can be produced by intracardiac injection of tubercle bacilli in the sensitized animal.

DR. GEORGE C. WELLS (by invitation): I very much appreciated the discussion of this case. I realize that the evidence for papulonecrotic tuberculid is incomplete, but it is difficult to find a satisfactory alternate diagnosis. While the biopsy made from a recent lesion showed only a circumscribed necrotic abscess, it should be noted that in 1950 a biopsy made from a scaling lesion of the breast showed a tuberculoid histology. I thought that this case might fit into the group of tuberculids described by Crocker under the name "acrodermatitis pustulosa hiemalis," since the winter recurrence is such a striking feature in this case.

As regards Dr. Michelson's suggestion of this being an "id" reaction to fungus infection, the intradermal reactions to histoplasmin and coccidioidin were negative.

Subacute Lupus Erythematosus. Presented by DR. THEODORE CORNBLEET, DR. DAVID COHEN and (by invitation) by DR. STEFAN BIELINSKI.

DISCUSSION

DR. LOUIS A. BRUNSTING, Rochester, Minn.: Traditionally, for more than a century, dermatologists have been identified with the subject of lupus erythematosus, the systematic classification of the disorder, research on its various phases, and the bulk of the responsibility of the management of the patients over the years. Significant contributions have recently come from other fields, making us realize that disease is never the province of a single specialty. We should maintain a constant awareness of these advances and cooperatively apply them to the benefit of the patient as a whole, or we may lose our respected position by default.

The four patients presented today demonstrate well the many facets of the problem of lupus erythematosus. It happens that in each instance the skin was involved. Such is not always the case. In dealing with systemic lupus erythematosus, for example, the experience of myself and my colleagues over the past several years indicates that often, perhaps in half the patients, the cutaneous features are minimal, transient, atypical, or absent altogether. The diagnosis rests on the ensemble, not on a single laboratory test, and may not be confirmed until necropsy findings are at hand.

Systemic lupus erythematosus is always a serious disease. There is no absolute index to prognosis, although the situation is at its worst in the case of the two young women who showed fulminating symptoms of sudden onset, with high fever, effusions, renal impairment, and purpura. A very high sedimentation rate of the erythrocytes, panhematopenia, reversed albumin-globulin ratio, and a strongly positive Hargraves' phenomenon make a characteristic laboratory picture. In these cases the outlook is poor. Signs and symptoms may be suppressed for the time being by cortisone or corticotropin (ACTH), but such treatment only delays the inevitable and is often not justified. On the other hand, the course of the disease in older women and in men is quite unpredictable. I have seen instances in which patients of this group have manifested relapses and remissions over periods of many years. The patient with systemic lupus erythematosus is engaged in a duel of reaction involving processes of immunity little understood; he may succumb to procedures we introduce under the guise of treatment. In general, I favor supportive and expectant management, with emphasis on bed rest and acetylsalicylic acid (Aspirin).

The two older women with lesions of discoid lupus erythematosus are in a different category. They show little systemic reaction or constitutional involvement; they are meeting the challenge of the disease very well, except for the cosmetic disfigurement. In their case, I believe treatment by means of the administration of strong iodine solution U. S. P. (Lugol's solution) or quinacrine hydrochloride (Atabrine hydrochloride) would be sufficient.

DR. HENRY E. MICHELSON, Minneapolis: I have treated 42 patients with quinacrine hydrochloride and have watched them carefully. I have confined the treatment strictly to patients given a diagnosis of the chronic localized discoid type. I have not had the uniformly good results that some report, but in the main the drug has been valuable. I found that those who were going to derive benefit seemed to show benefit quickly, long before they became pigmented. I stopped treatment the minute I though the improvement had come to a standstill. I have seen only a few cases of untoward signs, and in those instances I stopped the treatment at once. I think pigmentation without improvement in the lesion is

reason enough to stop the treatment. I doubt if the pigmentation is an index to the efficacy of the drug. I do not think we should continue administration of quinacrine hydrochloride over a long period. If the patient does not get results in three weeks, I think the drug should be stopped. I also, in the hospital, have tried the drug on what might be called subacute lupus erythematosus, and I was astonished to find that some of the patients bear the drug very well, with improvement. We have also given one patient who had gone through an acute phase and had responded to cortisone (Cortone) acetate a subsequent course of quinacrine hydrochloride. I do not know whether this is a good scheme or not or whether it is valuable. We have not had time enough to know.

DR. HAMILTON MONTGOMERY, Rochester, Minn.: In my article in "Oxford Loose-Leaf Medicine," written some years ago, one-third of the cases of chronic discoid lupus erythematosus eventuated in disseminated lupus erythematosus, which we now refer to as systemic lupus erythematosus. In the group of cases that Dr. Brunsting studied recently, there were many patients for whom a diagnosis was established by the L.E. test and in whom there never were any cutaneous manifestations. It is therefore understandable that in Dr. Brunsting's recent series the percentage of patients with systemic lupus erythematosus who started out having the chronic discoid type was much less than in my earlier series. The histologic changes in the skin in lupus erythematosus, whether of the chronic discoid or the acute systemic type, are distinctive if a lesion has been present for six weeks or longer. The transitory erythemas that may be encountered in acute systemic lupus erythematosus usually will not present a diagnostic histologic picture.

DR. GEORGE C. WELLS (by invitation): The case I mentioned was that of a 34-year-old woman with disseminated skin lesions of lupus erythematosus (widespread sunburn-like erythema and scaling of the face, neck, and arms) and with limited systemic involvement (borderline leucopenia, raised erythrocyte sedimentation rate, and slight albuminuria). She was treated with 0.2 gm. quinacrine hydrochloride daily, and after three weeks the eruption had disappeared, and she felt very much less tired. Her doctor has more recently reported that about two months after administration of quinacrine hydrochloride was discontinued there was some reappearance of skin lesions of the face.

We have recently seen a 9-year-old child with patchy lupus erythematosus on the face and arms, persistent fever over many months, high sedimentation rate, lymphadenopathy, albuminuria, and slight leucopenia. She was treated with quinacrine hydrochloride, 0.3 gm. daily, and responded well, remaining free of rash and fever through the winter, and over the last five months, since discontinuing administration of quinacrine hydrochloride, there has been no relapse, though the albuminuria remains severe. I certainly do not recommend quinacrine hydrochloride for systemic lupus erythematosus, but its use may be justified in some cases.

DR. THEODORE CORNBLEET: These two patients show that, as far as Cook County Hospital is concerned, we dermatologists no longer bear the responsibility for the care of acute lupus erythematosus. I found the two patients by visiting medical wards. The officers in the examining room who distribute incoming patients among the various departments cannot understand how the skin specialist could possibly be interested in or equipped to deal with patients whose sickness is systemic.

Our male patients with acute and subacute lupus erythematosus seem to show a more continuous course until death. They tend not to have the abrupt and spectacular remissions with or without cortisone and corticotropin that women more often have. Two of our male patients with discoid forms and arthralgias improved as far as their joints were concerned while on quinacrine hydrochloride treatment, though the skin lesions remained unmoved.

What should be our attitude toward castrating the patient with lupus erythematosus? Apparently there is no conclusive evidence that such an extreme measure cures or even helps. It would seem that a better case could be made out for removing the adrenals, because desoxycorticosterone acetate in proper concentration is known to be able to have an adverse effect on collagen. The patient would have to carry on with cortisone and, of course, corticotropin would thenceforward be useless.

Postinflammatory Hyperpigmentation. Presented by DR. GEORGE C. WELLS (by invitation).

History.—A. B., a 68-year-old retired carpenter, Italian by birth, beginning in June, 1952, had a severe dermatitis of the exposed parts, which gradually gave place to the extreme melanoderma that is now present.

In January, 1952, a combined abdominoperineal resection was done for adenocarcinoma of the rectum, and he now has had a colostomy.

For 18 months he has had paroxysmal auricular tachycardia, which has been controlled with quinidine sulfate, and he now takes 0.2 gm. of quinidine sulfate daily. In February, 1952, he had a transient rash on the legs, which he related to irritation from wool stockings.

The skin eruption started in June, 1952, when he was working on the roof of a house and was exposed to wood dust and to bright sunshine. He got what he thought was sunburn of the exposed parts, but, instead of getting better, the skin got itchier and more swollen and redder.

Physical Examination.—When first seen by us in August, 1952, he had a dusky red subacute eczematous dermatitis of the scalp, face, neck, and arms, which stopped abruptly at the covered parts. Besides scaling and edema there was some lichenification on the arms and ectropion of the lower lids. Lymph nodes draining the head and arms were enlarged.

Clinically there was evidence of arteriosclerotic cardiovascular disease.

Laboratory Findings.—Laboratory data were as follows: white blood cell count 5,700; with polymorphonuclear leucocytes 84%, lymphocytes 12%, monocytes 4%; hemoglobin 11.2 gm.; Kahn test negative; no albumin, no sugar, no abnormal amount of porphyrins in 24-hour urine specimen.

Roentgenologically there was a moderate cardiac enlargement, but lung fields were clear.

A biopsy of a specimen of the skin from the left arm on Aug. 19, 1952, showed some parakeratosis and edema of the epidermis, with enlargement of the interpapillary processes. The dermal papillae were edematous and contained a chronic inflammatory infiltrate which extended into the subpapillary corium. There was accummulation of pigment in melanophores in the upper corium and dilatation of small blood vessels.

Subsequent Findings.—The dermatitis slowly subsided during the latter part of the summer. He returned to the hospital in December, 1952, on account of herpes zoster of left thoracic 11th and 12th nerve distribution. X-ray of the thoracic spine revealed gross osteoarthritis but no evidence of metastasis. We were struck by the intense pigmentation in the areas previously affected by the dermatitis, the appearance being reminiscent of pellagra.

At present he shows over the face, neck, and arms, ending abruptly at the line of the shirt, a deep brown pigmentation, and now in some areas small islands of depigmentation are appearing. The herpes zoster has healed, though he is still being treated for postherpetic pain. There is some residual lymphadenopathy in the neck.

A biopsy was performed on a specimen from the left forearm on Jan. 19, 1953, through an area showing hyperpigmentation and depigmentation.

At the hyperpigmented end of the section there is accumulation of melanin in the basal layer of the epidermis, and there is some melanin in the melanophores in the upper dermis.

At the other end of the section pigment is absent from the epithelium, which is thinned. In the upper corium here there is vasodilatation and a lymphocytic infiltrate close under the epidermis.

Case for Diagnosis (Reticulated Melanosis?). Presented (by invitation) by DR. WALTER KLAK and DR. ALLAN L. LORINCZ.

History.—R. W., a 45-year-old mulatto housewife and solderer has for the past 15 years had reticulated hyperpigmentation distributed in collar fashion about the neck. About 10 years ago the skin over the upper extremities became dry and somewhat itchy and scaly. Then about 3 years later a finely reticulated hyperpigmentation developed in these areas.

During the summer of 1951, right radical mastectomy was done for carcinoma of the breast. The regional lymph nodes showed lipomelanotic reticular hyperplasia but contained no metastatic carcinoma. Surgery was followed by x-ray therapy, after which the melanosis on the right side of the neck became intensified. In the autumn of the same year, serum hepatitis developed.

Biopsy of a specimen from the liver was done and showed old portal cirrhosis, in addition to acute hepatitis. After the hepatitis and associated jaundice cleared, liver-function tests were found to be normal. However, following this episode of hepatitis, additional areas of the skin over the lower extremities and buttocks became itchy, dry, and slightly scaly and then went on to also develop the reticulated hyperpigmentation. A number of proprietary skin remedies have been used by the patient from time to time for skin discomfort.

Physical Examination.—Physical findings, except for the skin changes and surgical scars, was not remarkable. The skin about the neck, buttocks, and upper and lower extremities was asteatotic and slightly scaly. Most conspicuously, however, there was a finely reticulated hyperpigmentation over the areas.

Laboratory Findings.—Routine urinalysis, blood counts, chest roentgen examination, and Kahn test have all been normal.

Histologically specimens for biopsy from an involved skin area on the left arm show heavy pigmentation of the epidermal basal layer, together with some vacuolation. In the upper corium there are many melanin-laden phagocytes. In one area the epidermis appears flattened and atrophic.

DISCUSSION
OF CASES OF DR. WELLS, AND DR. KLAK AND DR. SORINCZ

Dr. Arthur C. Curtis, Ann Arbor, Mich.: I certainly do not have the answer to these two cases, but they allow at least some speculation, because there are some common factors in both. The carpenter in whom erythema developed and then pigmentation in the summer while building his son-in-law's house might have a tar melanosis, though he denied any contact with tar. There is one disturbing factor, since he had pigmentation of the mouth coming on six months after he was operated on for an adenocarcinoma of the colon. One wonders whether the adenocarcinoma played any part in developing the pigmentation. The extensive studies of Dr. Helen Curth on acanthosis nigricans and its relation to adenocarcinoma is recalled. There has been described by Yater polyposis of the colon and pigmentation of the mouth. One wonders whether Dr. Well's patient had polyposis of the colon, which led to malignancy and which in turn led to the photosensitization and pigmentation.

Likewise, in the case presented by Drs. Klak and Lorincz, this woman had a dermatosis very much like poikiloderma of Civatte, but the patient says the lesion began as an erythema and pigmentation followed. The pattern was reticulated. She had a carcinoma removed from her breast, and following removal infectious hepatitis developed, and following that pigmentation developed. One must wonder whether the carcinoma or the hepatitis had something to do with the pigmentation.

Dr. S. W. Becker: In the case of the Italian, I think he had photosensitization before the melanosis developed. I questioned him about various things he uses. I could elicit nothing that was a common sensitizer, but there may have been many things used in the building of the house he has forgotten about. His melanosis is of great interest, because it is really a leucomelanoderma. Developing on his hands are lesions which are typical of vitiligo. In the literature many lesions diagnosed as vitiligo have really been those of leucoderma.

The other patient, the mulatto, shows a subacute dermatosis which recurs in winter and gets better in summar. It suggests a parapsoriasis of some type and produces little itching. I think it could be poikiloderma, but I believe it would be poikiloderma of Jacobi rather than of Civatte.

Dr. Harold Shellow: I note in the history of Dr. Well's case that the patient had received over a period of 18 months quinidine sulfate for a cardiac disorder. I would like to ask the presenter if he thought there is anything to increased light sensitization that might exist from the use of quinidine sulfate over this long period.

Dr. George C. Wells (by invitation): We seriously considered quinidine sulfate as a possible photosensitizing substance in this case, and we tried to discontinue it, but the patient immediately got a severe tachycardia, and administration of quinidine sulfate had to be continued. The 24-hour specimen of urine collected soon after the outbreak of the eczematous light-sensitive eruption showed no excess of porphyrins.

I agree with Dr. Becker that this is now a leucomelanoderma, though the depigmentation has appeared only recently. I was surprised at the apparent atrophy in the white patches, and the histology here was somewhat reminiscent of poikiloderma.

The carcinoma of the colon was excised about six months before the light-sensitive eruption appeared. There was no polyposis of the part of the colon operated upon, and the carcinoma was considered to be a very early one; in fact, the pathologist hesitated to label it malignant. Certainly the surgeon thought it unlikely that the carcinoma had extended beyond the part excised, and on the whole it is improbable that there is any relationship between the carcinoma and the pigmentation in this case. It is nonetheless remarkable that our two patients with peculiar pigmentation had been treated for carcinomata.

Papular Myxedema (Papular Mucinosis.) Presented by DR. ALEXANDER M. BUCHHOLZ.

History—Mrs. V. V., a 26-year-old white woman, gives a history of an asymptomatic gradually spreading eruption for the past two years. Past history reveals arthritis for the past three years and for the past year anorexia and fatigue, with a weight loss of 11 lb. (5.0 kg.). Her family history reveals that her mother and two paternal aunts had thyrotoxicosis and thyroidectomies.

Physical Examination—The patient presents a generalized eruption of 2- to 100-mm.-sized papules, many of which are annular with depressed centers and borders which are pink to yellow and in some instances exhibit telangiectasia.

Laboratory Findings—Laboratory data were as follows: red blood cell count 4,470,000; hemoglobin 78.8 gm.; color index 0.9; white blood cell count 4,200, with neutrophiles 62%, lymphocytes 31%, eosinophiles 3%, transitional cells 4%; blood sugar 130 mg.; basal metabolic rate +6; sedimentation rate 18 mm. in one hour; cholesterol 190 mg.

Biopsy showed typical mucin in the upper dermis, with young connective tissue cells.

DISCUSSION

DR. J. E. DALTON, Indianapolis: The lesions shown by this woman resemble those seen in a man Dr. James Engeler presented before this Society. The two cases exhibited small- to medium-sized papules having an elevated peripheral ring and a sunken central zone. The lesions differ somewhat from the evenly domed or flat papular elements seen in the woman with lichen myxedematosus, whom I have observed over a 14-year period. However, these three cases and the other few reported examples of this entity show the common findings of mucinous deposits in the skin, freedom from detectable thyroid disease, and absence of other physical and laboratory findings to explain their causation. For the present we can only say that these cases belong to a lately delimited entity whose etiology is unestablished.

Since these particular cases show neither a demonstrable hypo- nor hyper-thyroid state, it seems inadvisable to continue to group them under a diagnostic designation which stems from the word myxedema. Palitz and Brunner have lately recommended the use of the term mucinoses for all mucin-containing skin diseases, and under this general heading they established subgroups for the various associated entities. This thought was accepted with modifications in a paper to be published by myself and Dr. Seidell, and we chose to list these particular cases as papular mucinosis.

DR. HAMILTON MONTGOMERY, Rochester, Minn.: Dr. Dalton, with the collaboration of Dr. Seidell, presented a paper at the American Dermatological Association last year on lichen myxedematosus (papular mucinosis) (A.M.A. ARCH. DERMAT. & SYPH. **67**:194 [Feb.] 1953).

I presented two cases and reported four others before the meeting of the Society of Investigative Dermatology, in June, 1952, with the collaboration of Underwood (*J. Invest. Dermat.* **20**:213, 1953). Dr. Fred Weidman and I had the opportunity of studying the histologic findings in Dalton's case, which was first presented in 1940. We used the term generalized localized myxedema at that time, but it is not a good one, as these patients have no evidence of endocrine distubance. The case presented by Buchholz did not appear to show mucinous changes with hematoxylin and eosin stain, but I did not have the chance to study the sections stained for mucin. The patient presented has definite lesions of lentigines.

In regard to lichen myxedematosus, one of my patients died, and postmortem examination failed to reveal any evidence of myxedematous changes in any of the internal organs, or was there any evidence of scleroderma. Some of these cases have been misdiagnosed as xanthoma, others as nitidus, and others as papillary scleroderma. The erroneous diagnosis of scleroderma results, I believe, from mucinous edema of the digits and mouth, causing stiffness of the fingers and tightness about the mouth simulating acrosclerosis. There is neither homogenization of the connective tissue bundles nor obliterative changes in the smaller vessels, such as one sees in true scleroderma. I have gone over a good many cases of scleroderma of different types without being able to demonstrate mucin in the tissues.

I therefore believe that lichen myxedematosus is a definite entity and not related to scleroderma, on the one hand, or to endocrine disturbance, including myxedema, on the other hand.

DR. M. R. CARO: For reaching a prompt diagnosis in the present case we are all indebted to the patient whom Dr. Engeler showed before this Society in February of last year. Dr. Szymanski and I studied sections from Dr. Engeler's case, and we found central fibrosis with a zone of mucin on either side. When Dr. Buchholz sent in his specimen, we both recognized the sections as being identical with the changes seen in the case of Dr. Engeler. There was central scarring, with mucin present on either side in the upper corium. Because the tissue was fixed in formalin, the stain for mucin has largely disappeared. We are going to obtain another specimen in absolute alcohol so that the stain for mucin will be more lasting. I do not think that these cases have any relation to the cases reported recently by Dr. Dalton and Dr. Montgomery. The lesions here have a doughnut appearance, with central scarring, and there was no evidence of such lesions in the other cases reported.

DR. A. M. BUCHHOLZ: I am indebted to Dr. Caro for the diagnosis. On receiving the diagnosis I became very interested and searched the literature. We find that the first such case was described in 1916 by Jadassohn. In his article he described cases that were oval to round disseminated papules, 2 to 10 mm. in size, which evolved into annular lesions with atrophic centers. I feel that this case is typical of this type. Searching the literature, little was found until 1921, when Freudenthal presented a case which resembled this and submitted this classification: (1) myxedema found in cretins with definite thyroid dysfunction; (2) pseudo-tubular type of myxedema, which is often associated with thyroid dysfunction; (3) papillary type of lesions, which are papular tubercles and lichenoid lesions, which fall into the group of cases such as I presented, none of which have anything to do with thyroid dysfunction. Certainly, we should try to group this type of case with the one Dr. Engeler has shown.

Papulonecrotic Tuberculid. Presented (by invitation) by DR. GEORGE C. WELLS.

Lupus Erythematosus: Fixed Type Treated with Quinacrine Hydrochloride (Atabrine Hydrochloride). Presented by DR. JAMES H. MITCHELL.

Discoid Lupus Erythematosus of Erythema Perstans Type with Severe Rheumatoid Arthritis. Presented (by invitation) by DR. ALLEN L. LORINCZ.

Acute Lupus Erythematosus. Presented by DR. THEODORE CORNBLEET, DR. SIDNEY BARSKY, and (by invitation) DR. J. F. SICKLEY.

Case for Diagnosis (Sebaceous Cyst?). Presented by DR. JAMES H. MITCHELL.

Scleroderma. Presented by DR. JULIUS E. GINSBERG.

Scleroderma (Acrosclerosis). Presented by DR. DAVID OMENS and (by invitation) DR. HAROLD OMENS and DR. STEFAN BIELINSKI.

Case for Diagnosis: Generalized Sweat-Gland Inflammation? Presented (by invitation) by DR. H. M. SHAIR, Quincy, Ill.

Tinea Capitis in Healthy Woman of Thirty-Two. Presented by DR. HERBERT RATTNER.

Mycosis Fungoides. Presented by DR. HERBERT RATTNER, DR. HAROLD RODIN, and (by invitation) by DR. STEFAN BIELINSKI.

Clinical Mycosis Fungoides, d'Emblée of Inverse Type (with Histological Picture of Lymphoblastoma). Presented by DR. JAMES WEBSTER, DR. STANLEY HUFF, and (by invitation) by DR. J. F. SICKLEY.

A Case for Diagnosis. Presented by DR. DAVID OMENS and (by invitation) by DR. HAROLD OMENS and DR. J. F. SICKLEY.

Hodgkin's Disease with Trophic Changes (Ichthyosiform Atrophy—Loss of Eyebrows and Axillary Hair). Presented by DR. SAMUEL BLUEFARB, DR. AARON GOLDBERG and (by invitation) by DR. J. F. SICKLEY.

Argyria. Presented by DR. DAVID OMENS and (by invitation) by DR. HAROLD OMENS and DR. STEFAN BIELINSKI.

Chancroid. Presented by DR. THEODORE CORNBLEET, DR. HENRY SCHORR and (by invitation) by DR. STEFAN BIELINSKI.

NEW YORK ACADEMY OF MEDICINE, SECTION ON DERMATOLOGY AND SYPHILIS

Marion B. Sulzberger, M.D., *Chairman*

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Nov. 6, 1952

Leprosy, Lepromatous Type: Response to Isoniazid Therapy. Presented by Dr. William Director and Dr. Roman Lysiak.

This patient, W. Q. C., was admitted to the hospital on July 3, 1952, because of pea-sized and smaller infiltrated nodules on the face (especially on the nose), extremities, and buttocks. The lesions started to appear on the left cheek one year (?) before admission and gradually the process spread over the other surfaces of the skin.

Treatment consisted of administration of isoniazid (Rimifon), 150 mg. daily from July 10 to Aug. 25 (in total, 7 gm. and 50 mg.) and an isopropyl derivative of isoniazid (Marsilid), 150 mg. daily from Aug. 26 to Nov. 6 (in total, 10 gm. and 650 mg.).

There has been definite improvement; numerous nodules diminished in size, and some disappeared completely.

Laboratory findings on admission were as follows: A blood cell count gave the following results: red blood cells, 4,590,000 per 100 cc.; white blood cells, 11,300; hemoglobin content, 13.5 gm., and a differential distribution of 6/62% polymorphonuclears, 23% lymphocytes, 5% monocytes, and 4% eosinophiles. Mycobacterium leprae were found in abundance in a tissue smear from the ear lobe and from a lesion. (Last tissue smear from the lesion on the forearm on Oct. 27 showed a strongly positive reaction too). The Mazzini and the Wassermann tests both gave a 4+ reaction. The erythrocyte sedimentation rate by the Westergren method was 58 mm. in one hour. Nonprotein nitrogen was 33 mg. Urinalysis revealed a trace of albumin. Cephalin-cholesterol flocculation gave a 4+ reaction. Albumin-globulin ratio was 4.3/4.5 gm.; chlorides, 100 mg.; cholesterol, 244 mg.

The pathological diagnosis was granuloma consistent with the diagnosis of lepromatous leprosy.

Tuberculoid Leprosy. Presented by Dr. Jack Wolf, for Dr. Max Braitman.

N. P., a 14-year-old Puerto Rican girl, residing in the United States for the past eight months, was first seen at the New York Skin and Cancer Unit on Aug. 28, 1952. She gave a history of a gradually spreading eruption of approximately 10 years' duration. The information that the father is suffering from an eruption was elicited, but thus far we have been unable to get the father to come to the clinic for examination.

On examination, the patient presents many larger and smaller depigmented rounded and roughly oval-shaped patches, with dry slightly thickened hyperpigmented and erythematous borders. The locations involved are chiefly the posterior aspect of the trunk, the abdomen, the thighs, and the shoulders. Only a few of the lesions are symmetrically placed. The ulnar nerves are thickened. There is moderate contracture of the left ring and little fingers. There is definite diminution of sensation in the affected areas.

Histologic examination by Dr. A. B. Hyman revealed the following findings: Tuberculoid structure consistent with leprosy was revealed. Bacilli were not found in the sections examined. The lepromin test gave a negative result; the histamine test gave a positive result. Four nasal smears showed a negative result for acid-fast bacilli. The serological reaction for syphilis was negative.

The patient was given isoniazid (Rimifon), 50 mg. three times daily, on Oct. 2. After two weeks of treatment the lesions appeared less elevated; otherwise there was little change. The patient has tolerated the medication very well to date.

DISCUSSION ON CASES OF LEPROSY

Dr. A. A. Fisher: The case of Dr. Wolf, in which the patient had tuberculoid leprosy, demonstrated beautifully the histamine reaction. Intradermal injections of histamine showed no flare in the involved area, whereas in the adjacent normal skin there was the usual flare with the histamine.

DR. ORLANDO CANIZARES: I think that the small boy demonstrated the fact that leprosy is a disease of childhood, that it is usually acquired in childhood. Although the period of incubation may be long indeed, it does not appear until later in life, but in some it develops early. Infants are rather immune to leprosy. After they reach the age of 1 or 2 the lesions may start developing. I shall not say that they are immune, but with the period of incubation required they are free from it for some time. The small boy represents the type that is a classic example of what we call the measured tubercle, large areas with the border presenting very tiny shiny papules.

As far as treatment is concerned, the isoniazid preparations seem to help to a certain extent in the lepromatous type, but it is my experience that in the tuberculoid type the results are very poor.

DR. JOHN GROOPMAN: I should like to say that when we contacted men at the Hoffmann-LaRoche, Inc., laboratories about their experience with tuberculous patients being treated by their preparation, we learned that they feel that the side-effects can be reduced by combining the isoniazid and the isopropyl derivatives of isoniazid groups together, pushing in a greater amount per kilogram of weight. With that they have less side-effects. This observation has been supported in some of the hospitals and institutions upstate.

DR. TANCREDO A. FURTADO, Brazil: I should like to make a comment on the case presented by Dr. Wolf. In my state (Minas Geraes) we have over 10,000 cases of all forms of leprosy and six leprosaria. That case interested me very much by the fact that the lepromin reaction was negative. According to the South American classification, which was adopted in the last International Congress in Habana, the cases of the tuberculoid leprosy generally present positive lepromin reactions, showing good response of the organism, which reacts well in the presence of the disease, and with no bacilli being shown in the sections or in the nasal scrapings. If the tests show negative reaction, then we have two possibilities: either lepromatous leprosy or undeterminate leprosy with the tendency toward lepromatous leprosy. So I suggest that another Mitsuda-Rost, or lepromin, test be given that patient, because from the point of view of prognosis it is important that the case be exactly classified. A negative result to the lepromin test shows a bad prognosis, and the patient should probably be hospitalized. I do not know if Dr. Wolf made the 48-hour tuberculin type of reaction, which is sometimes not very valuable, or the late Mitsuda-Rost reaction, which should be read two or three weeks after the intradermic test has been performed. I must apologize for talking too much, but these facts assume importance from the point of view of prognosis and epidemiology.

DR. WILLIAM DIRECTOR: An interesting point in therapy has been raised, judging the effect of a medication, such as the isoniazids. We see very few patients with leprosy, so we cannot render very hard-and-fast judgments as to whether or not this is a spontaneous recovery, as has been known in lepromatous leprosy, or whether this is a real response to medication. The response has been very slow, but it has been very real. As I understood, there are rather conflicting opinions among those who see large numbers of patients with leprosy, some feeling that the isoniazids are effective and others that they are not. This patient is not a very good example for either viewpoint. Organisms are still present in the lesions.

Epitheliomata, Multiple, Basal-Cell Type, of the Face and Forehead Treated with Thorium X. Presented by DR. A. J. ORFUSS and DR. S. ROBBINS.

B. T., a woman aged 38, was presented before this section on Nov. 7, 1951, prior to treatment, because of the widespread dissemination of the lesions, with histopathologic findings of basal-cell epitheliomata. One lesion was destroyed by desiccation and curettage. The other lesions and newly developing ones were treated with thorium X solution (alcoholic, 2,000 electrostatic units [E. S. U.] per cubic centimeter) (300 mμ per cubic centimeter). Total treatments given were eight treatments at weekly intervals to four lesions of the upper forehead. Five treatments at weekly intervals to the lesion of the left side of the nose and eight treatments at weekly intervals to the lesion of the right paranasal area were given.

Examination as of Oct. 30, 1952, revealed a new match-head-sized nodule on the right cheek which has the clinical character of the previous lesions.

The disease has been present for four years.

DISCUSSION

DR. W. H. WARD, Australia: I am quite satisfied that this particular type of case is nevoid in origin. A statistical survey in our clinic showed that among immigrants to our country it took an average of 44 years' residence before carcinomatus lesions would develop. However, a few cases were found in which the patient's sojourn in Australia was for only a short time. These patients were much younger than the average of all the patients, and all gave a family history of relatives with similar lesions. This patient states that two members of her family are similarly affected. I consider this to be a nevoid type of basal-cell carcinoma.

DR. JUAN LARRALDE: This case was presented to this society last year, and I raised exactly the same question. I think that the lesion is trichoepithelioma, a benign condition. I do not think that it is a real basal-cell epithelioma.

DR. VICTOR HERBERT WITTEN: I think that this is an example of a satisfactory response of a basal-cell epithelioma to thorium X treatment. In other cases of superficial basal-cell epithelioma as well use of thorium X has proved to be an excellent method of treatment, with no evidence of scarring being found afterward. Such is the case in this lesion, which was on the face. (Witten, V. H., and Lazar, M. P.: Multiple Superficial Benign Basal-Cell Epithelioma of the Skin, *Brit. J. Dermat.* **64**:97, 1952.)

DR. MARION SULZBERGER: The histology is described as basal-cell epitheliomata. May I ask Dr. Ward whether, when he was referring to his cases, he meant basal-cell epitheliomata and trichoepitheliomata?

DR. W. H. WARD, Australia: Yes.

DR. PAUL GROSS: The possibility of a nevoid anlage has been under discussion ever since the multiple basal-cell epitheliomata were first recognized. The histopathologic findings of so-called multicentric epitheliomata in these cases has been used as an argument in favor of a nevoid nature. On the other hand, Ayres and Andersen have shown that the same clinical picture of multiple basal-cell tumors can also be produced by chronic arsenical retention. The differential diagnosis from trichoepitheliomata is neither clinically nor histopathologically difficult.

DR. MARION SULZBERGER: I should like to point out that I think that the main object, or one of the main objects, of this presentation was to demonstrate the effectiveness of treatment with thorium X. I hope that Dr. Orfuss and Dr. Robbins will, in closing, tell us something about that aspect—the therapeutic aspect.

DR. S. J. ROBBINS: I should prefer that Dr. Orfuss or Dr. Witten discuss the subject of thorium X, but may I state that we took numerous specimens for biopsy? Morphologically, the lesions never impressed us as being basal-cell epitheliomata. They looked more like trichoepitheliomata, and they seemed nevoid in character, but histologically they were always basal-cell epitheliomata.

DR. A. J. ORFUSS: The treatments were given exactly as they were outlined. Some of the lesions received as many as eight applications. Others got five applications, all at weekly intervals. The strength of the solution was 2,000 E. S. U. per cubic centimeter. The manner of application consisted of first defatting the skin by carefully washing it with a fat solvent, such as acetone, and then by careful application of the solution to the lesion at five intervals. After the application of this solution—after five applications had been made—the lesion was allowed to dry, and then a coating of flexible collodion was applied and allowed to dry on the lesion. About the second or third week the lesion becomes very red, and the redness persists until after the treatment is finished.

The slides that were presented with the patient showed the patient before treatment, and during treatment, and, of course, you were able to see the after-treatment results. Dr. Witten can probably discuss the penetrability of the thorium X solution much better than I can.

DR. VICTOR HERBERT WITTEN: I do not think I need discuss the penetrability of thorium X before this audience. That it does penetrate human skin has been demonstrated. (Witten, V. H.; Ross, M. S.; Oshry, E., and Hyman, A. B.: Studies of Thorium X Applied to Human Skin, *J. Invest. Dermat.* **17**:311, 1951.)

Case for Diagnosis: Xeroderma Pigmentosum? Presented by Dr. Jack Wolf for Dr. H. S. Appell.

C. S., a Negro woman, aged 52, is presented from the New York Skin and Cancer Unit with a generalized eruption of five years' duration. In her history it was elicited that her father was white, her mother Negro, and her grandmother Indian (American). Her health until the onset of the present trouble was good. She recalled no special medical care, except that for a two-month period in 1934 she had received injections for arthritis.

The present condition first manifested itself suddenly some five years ago, with the development of pigmented and depigmented spots on various parts of the body. As the eruption spread, she also became aware of the fact that she was extremely sensitive to sunlight and that her eyes began to tear immediately on exposure to the sun's rays. The eruption, the photosensitivity, and the pruritus have been getting progressively worse. Thickened, hyperkeratotic and verrucous lesions have been developing at various sites.

On examination, the patient presents a generalized pigmented and depigmented eruption, with areas of depigmentation varying in size from small match-head-sized spots to large irregularly shaped confluent patches. The various folds of the body are hyperpigmented, without any evidence of depigmentation. Smaller and larger hyperkeratotic and verrucous lesions are present on the head and neck, the upper aspect of the chest, and, to a smaller degree, on other parts of the body. Small ulcerated lesions of recent origin are present in various locations, chiefly the exposed parts. The palms are thickened and hyperkeratotic.

Ophthalmologic examination, on May 16, 1952, revealed cicatricial ectropion, attributable to the eruption.

Laboratory examinations gave the following results: Urinalysis, done on May 13, gave normal results. The serologic reaction for syphilis on April 29 was negative. The icterus index, on May 1, was 417 units (normal, 4 to 6). Blood studies taken Sept. 25 gave the following results: red blood cells, 4,100,000 per cubic millimeter; hemoglobin content, 8.7 gm. per 100 cc.; slight anisocytosis and slight achromia; leucocytes, 6,800; polymorphonuclear neutrophiles, 55%; eosinophiles, 1%; lymphocytes, 42%; monocytes, 2%. Examination of the blood on July 18 both for porphyrins and for arsenic gave negative results.

Biopsies from pigmented keratotic and ulcerative areas were done. The totality of the three slides warrant a diagnosis of xeroderma pigmentosum. None of the three is frankly malignant. None of the three in itself shows a close picture of atrophic areas of xeroderma pigmentosum.

The biopsy report of July 24, by Dr. A. B. Hyman, gave the following findings: The microscopic diagnosis was no definite evidence of malignancy. There was marked hyperkeratosis in crust formation over a markedly acanthotic epidermis. There were a number of eosinophilic-staining cells present. There was a mild inflammatory reaction composed of small round cells, histiocytes, some plasma cells, and pigment-containing chromatophores high up in the cutis hugging the epidermis. There was a mild hyperkeratosis over an acanthotic epidermis which formed a network in one part. There was an inflammatory reaction high up in the cutis hugging the basal-cell layer.

DISCUSSION

Dr. David Bloom: Although it is possible for xeroderma pigmentosum to appear later in life, in this patient the eruption might well have been produced by liver disease. And, in fact, as the icterus index in this patient is as high as 400 units, one must seriously consider the possibility of the skin eruption being linked to the liver disturbance in this patient.

Dr. Arthur B. Hyman: I examined the slides. The diagnosis is offered under great pressure, but I do not think that there is any other diagnosis as good as that to offer to you. We all know that xeroderma pigmentosum is an inherited recessive disease, which ordinarily manifests itself in early childhood. This case would have to be put in the atypical group that arises in later life. The clinical features, rather than the history, fit in with xeroderma pigmentosum adequately, and she has the typical ectropion. In spite of the views of some histologists, who regard the microscopic picture of xeroderma pigmentosum as being almost pathognomonic, I do not think that to be the case. It depends upon which lesion one excises

as to what one is going to see under the microscope. The two or three biopsies performed on this patient gave pictures such as are found in some of the phases of xeroderma pigmentosum of the more classic type. Unless we have definite evidence of a more satisfactory diagnosis to offer, I think that of xeroderma pigmentosum should be accepted.

DR. CHARLES WOLF: In the first place, when one accommodates a diagnosis to the pathologic picture one is walking on rather dangerous and tenuous ground.

Firstly, I can dismiss the diagnosis of xeroderma pigmentosum with this terse statement, that, as far as I know or as far as is found in the literature, there has been no case reported among the Negro race.

Secondly, an interval of many years before the first manifestations of xeroderma pigmentosum appear is entirely unusual and probably does not occur. This patient gives a very plausible history of having had arthritis and of having been treated by injections. The supposition is that either gold or arsenic, or the combination of these heavy metals was used. It is rather consecutive in the history of metal poisoning that a long interval may appear before any manifestations of untoward effect are shown, and this fits in very well with the review of the history of the patient. She has had an interval during which she received her injections and then there was a long interim, after which the eruption appeared. All manifestations of the eruption from the clinical aspect indicate that it is an acquired disease, not a congenital disease.

Now, in order to corroborate the postulate, I believe that further studies ought to be made. Arsenical determinations should be made from the skin, as well as gold determinations. The keratoses on her palms are indicative of metal effect. My tentative diagnosis is arsenical or gold dermatosis.

DR. ELSE A. BARTHEL: I have nothing to add. I could not figure out whether her skin was turning black or whether it was turning white.

DR. DAVID BLOOM: Xeroderma pigmentosum in Negroes is no rarity. In fact, several such cases have been presented at this section in the past few years. Moreover, this patient is a very light-skinned Negro and descends from white and Indian ancestors. There is, therefore, no objection whatsoever to considering xeroderma pigmentosum as a possible diagnosis.

DR. ARTHUR B. HYMAN: Xeroderma pigmentosum has been reported in the literature as occurring in full-blooded Negroes in Africa, and not only in those of mixed races.

Secondly, as far as I know, arsenic is not used in the treatment of arthritis or rheumatism, so that if she had treatment for rheumatism the presumption is that she was given gold rather than arsenic. Gold may produce an acute or subacute dermatitis, in which state ectropion and other features of this case may be found, but gold would not result in a persistent dermatitis, 15, or 10, or even 5 years after the original eruption (of which we have no evidence), to produce the picture we see tonight.

DR. W. H. WARD, Australia: Xeroderma pigmentosum is a very rare disease in our country. This case is a fascinating one, and the patient states that the rash is equally distributed over the whole body, with no areas being spared. It is interesting to me that in light-sensitivity eruptions we find that the light-exposed areas, i. e., the arms, the face, and the V of the neck, are affected and that the rest of the body is clear, with the exception of the legs, which are sometimes also affected, although covered from light. This case I believe to be a toxemic one.

DR. JACK WOLF: We could not arrive at a definite diagnosis, and that is way we presented this patient for diagnosis. Actually, we did not attempt to fit either the clinical diagnosis to the pathologic one, or vice versa. We made the diagnosis clinically, at least we entertained that diagnosis, since we have not made a definitive diagnosis yet. The histologist felt that if there was any single diagnosis he could possibly make, it was that of xeroderma pigmentosum. Nevertheless, I could not reconcile myself completely to the diagnosis of xeroderma pigmentosum on account of (1) the age of onset, and (2) the fact that the patient is Negro. As has already been mentioned, xeroderma pigmentosum does occur in the Negro

race. In the *British Journal of Dermatology* there is a report of several cases of xeroderma pigmentosum occurring in Negroes, but these were all in children in whom the process had already started before they were 3 years old.

In regard to the question of arsenic, this patient has been questioned repeatedly, but we have never obtained a history of arsenotherapy. To the best of our knowledge, she has not received any arsenic. There is no history of syphilis. The serologic reactions for syphilis have all been negative. Urinary studies for arsenic on several occasions were not revealing. There is the possibility that this patient received gold therapy for arthritis. If she did receive gold, there was a hiatus of some 15 years, much too long a time for the development of this type of clinical picture. Depigmentation associated with metal chemotherapy occurs during or shortly after treatment.

We shall continue our studies in this case. If there is any finding of interest we shall report it to the section.

Case for Diagnosis: Linear Lichenoid Purpuric Dermatosis? Presented by DR. N. SOBEL, for DR. L. S. KLEEBERG.

In this little girl, E. B., aged 5, the oldest of three sisters, of whom the other two are healthy, a linear, hemorrhagic eruption on the right thigh and the leg suddenly developed, in October, 1951, without any subjective symptoms.

When first seen on May 9, 1952, at the skin and cancer unit of New York University-Bellevue Medical Center, the eruption consisted of a broad band of lichenoid erythrosquamous lesions which extended from the right buttock along the posterior aspect of the right thigh, the popliteal space, the outer side of the leg, and the dorsum of the foot to the medial aspect of the right foot.

Routine laboratory examinations, including a hemogram and study of blood chemistry, revealed no abnormalities.

X-ray examination of the lower spine showed no evidence of spina bifida. The histologic report by Dr. Charles S. Miller is as follows: "Epidermis is somewhat acanthotic. There is a marked bank of cellular infiltration, occasionally in the subepidermic zone and upper part of the cutis. This infiltrate is composed of round cells and wandering connective-tissue cells. Interspersed in this infiltrate are congested capillaries and occasional blood vessels. Some of the walls of these capillaries are broken, and there is hemorrhage right into the tissue. Perle reaction is positive for hemosiderin. Methylene blue stain for mast cells is negative. Histologic diagnosis—no definite histologic diagnosis. This condition suggests a vascular process, with hemorrhage into the tissue. There is no evidence of any epithelial or vascular nevus in all the slides studied."

During the five months that the patient has been under observation and treatment, practically no change has taken place. Some new spots have developed on the leg and sole. One spot has faded. The patient received rutin with vitamin C and vitamin B complex with iron.

DISCUSSION

DR. N. SOBEL: This child has an eruption which we do not want to classify as Gougerot-Blum disease, even though it is presented with a similar caption. We are unable to make a diagnosis. One of the things we have considered as a possibility is a nevus of some type, possibly distantly related to nevus unilateralis. Tonight I noted that there was also a lesion on the right side of the vulva and along the buttocks, so that the distribution of the eruption fits in better with such a condition. We do not think that it is inflammatory. It does not resemble lichen planus histologically in any way, so the only thing we can think of is something of the nevoid type.

DR. DAVID BLOOM: I wish to suggest that this is a case of Gougerot-Blum in linear form. Lichen planus, psoriasis, or lichen simplex may appear in linear configuration; so may any other dermatosis.

DR. JOHN GROOPMAN: I think that this case resembled the one that Dr. Combes and I reported a couple of years ago. The only difference from the Gougerot-Blum type and this case resolves itself in the absence of discrete small copper-colored types of hemorrhagic

points. The suggestion I would make, that might be very helpful, is to use an intradermal injection of one of the venoms, preferably moccasin venom (Agkistrodon piscivorus) to see if the same type of reaction would develop. The results of our test resembled the lesions of the dermatosis, giving us a clue to its apparent etiology. I suggest that that be done here to distinguish it from the nevus group.

DR. PAUL GROSS: The suggestion of doing a moccasin-venom test is a good one, but the test should be performed in the segment in which the dermatosis has occurred and in the normal skin of the corresponding segment on the other side. The eruption is not typical of Gougerot-Blum dermatosis, but it certainly belongs in this group, despite the fact that it is confined to a metameric segment.

DR. SAMUEL B. FRANK: I am curious to know what the character of that pigment is. Has any investigation been made in that direction? The lesions have a very peculiar coppery color.

DR. N. SOBEL: The Perle stain of the tissue was positive for hemosiderin.

DR. L. S. KLEEBERG: I do not believe this to be a case of Gougerot-Blum disease. No Gougerot-Blum disease in children nor unilateral cases have been reported so far. Also, the disease is commoner in men than in women.

The histologic examination which was done by Dr. Charles Miller gave a picture which was quite different from Gougerot-Blum disease. This case belongs to the group of linear dermatoses. Felix Pinkus (1902) stated that these lesions always follow the same pattern, not the so-called Voigt's internal boundary line—as suggested a long time ago—but Langer's lines of cleavage. Pinkus suggested that this line may represent a maximum or minimum of tissue tension.

Herman Pinkus mentioned these findings in his paper on lichen striatus and lichen planus.

Pemphigus Foliaceus: Response to Corticotropin (ACTH) and Cortisone; Appearance of Acanthotic Lesions. Presented by DR. WILLIAM DIRECTOR and DR. H. ROGACHEFSKY.

I. M., a man aged 58, was admitted to Bellevue Hospital on March 6, 1948, with a generalized exfoliating dermatitis and irregularly occurring scattered bullae and vesicles of several months' duration.

He was treated with carbarsone and paraaminobenzoic acid in 1948 and, subsequently, with quinacrine hydrochloride (Atabrine dihydrochloride), oxytetracycline (Terramycin), and sulfisoxazole (Gantrisin) in 1949. There was no improvement with these treatments. In late 1950 he was given intravenous chlortetracycline (aureomycin), and in 1951 sulfapyridine, again with no effect.

On Nov. 25, 1951, corticotropin (ACTH), a dose of 20 mg. daily, administered intravenously by slow drip, was started and was gradually increased to 80 mg. daily until March 5, 1952. With this regimen there was improvement in the form of less exfoliation and fewer bullae. Instead, dusky erythema was noted to appear, as well as a gradual appearance of numerous raised crusted adherent patches on the trunk and extremities.

Corticotropin gel, 160 mg. daily, was administered from March 19 to April 29, with little change in this picture.

Cortisone was then started, and a dose as high as 400 mg. daily was used, after which the dose was gradually decreased until it was 250 mg. daily on Oct. 21, 1952, and it has been maintained at this level to the present. With the corticotropin and steroid therapy of recent months there has been clearing of all bullae and most of the exfoliation, but the dusky erythema and the acanthotic areas have persisted.

Biopsies performed on Feb. 19, March 11, and May 6 all revealed pictures which indicated acanthotic epidermis and changes consistent with the diagnosis of pemphigus foliaceus.

DISCUSSION

DR. DAVID BLOOM: Not only in pemphigus foliaceus but also in pemphigus vulgaris and in psoriasis may one find in the course of treatment with corticotropin and cortisone the development of acanthotic-hyperkeratotic lesions. In one case of pemphigus vulgaris two such lesions persisted for a long time and finally disappeared. In a case of psoriatic erythroderma the upper and lower extremities were affected extensively in this way, but after a while the acanthotic eruption disappeared, although cortisone administration was continued.

DR. BEATRICE M. KESTEN: May I call on Dr. Brodey, our resident at Presbyterian Hospital? He can answer the question of whether any have been seen better than I.

DR. MARVIN BRODEY: I have never seen any similar lesions in our series of patients admitted for pemphigus.

DR. JOHN GROOPMAN: I should like to add that we must not confine these acantholytic nodules solely to pemphigus. We have seen them in other cases in which there was treatment with the cortisone and corticotropin. That they be not confined solely to this disease is a very important point. A little description is in order here. These nodules are small, almost the size of or slightly smaller than a split pea. They are dome-shaped. They seem to have that "stuck-on" appearance on the skin, and they are true acanthotic nodules, clinically by appearance and microscopically.

DR. PAUL GROSS: I do not believe that this development is confined to cortisone-treated patients with pemphigus. I have seen the development of multiple acanthomas recently in a patient with scars due to a third-degree burn in whom psoriasis also had developed at the site of the burn. The lesions underwent spontaneous involution after the psoriasis was cleared up. I saw another patient with multiple acanthomas on the dorsum of the hands which had developed after severe occupational dermatitis.

DR. WILLIAM DIRECTOR: In regard to the remarks of Dr. Gross, I have not noticed such reactions in anything but the pemphigus group. I do not refer to simple areas of thickening—hyperkeratosis, which can be the terminal stages of many types of dermatitis. This is a phenomenon that occurs in the resistant phase of pemphigus, chiefly pemphigus vegetans and pemphigus foliaceus. The lesions have been observed in patients prior to the treatment with corticotropin and cortisone. However, I do believe that they do occur more strikingly and more frequently now that we are seeing patients who make recoveries or at least have their lesions suppressed by this type of therapy.

This type of lesion should not be described clinically as acanthotic. It is a papule or nodule which looks warty. Microscopically, it is, however, a localized hyperplasia of epidermis, or acanthosis. This patient has had biopsies done at various stages of his disease, including the early stages of recovery. The earlier papules did show the same changes that one sees in pemphigus—splitting of the epidermis at a high level. Recently, the papule was completely dry, showing none of the changes of pemphigus. Since I have also seen this change in another patient with pemphigus foliaceus and similar changes in a patient recovering from pemphigus vegetans, I believe that this is a phase of resistance to pemphigus rather than an extraneous or casual finding. I think that it represents a partial resistance to the disease. Whether it occurs spontaneously in the disease or whether it occurs partly under the influence of corticotropin and cortisone, I do not know. The reason for presenting this particular patient was that he showed this phenomenon to a rather extreme degree. I doubt very much that had this patient been presented with an unknown case for diagnosis that anybody would have thought of the diagnosis of pemphigus foliaceus. This is not a specific phenomenon which occurs in pemphigus only, but is an indication of the resistance to the disease in these two cases, both of which show acanthosis or hyperplasia of the epidermis through all phases of the disease.

Case for Diagnosis. Presented by DR. JESSE A. TOLMACH.

I. C., a Puerto Rican woman, aged 49, presents crusted erythematous lesions covering the lips and extending from the nares to the chin. The patient stated that a year and a half ago the eruption started after a throat infection.

Scattered over the entire body are excoriated erythematous papules. Despite many types of therapy, including the use of antibiotics, x-ray, soothing ointments, and cortisone, there has been only a slight change in the condition.

The histological findings were as follows: Biopsy section showed an acanthotic mucous membrane covered by a pyogenic crust. The suprapapillary plates were very thin. The corium was filled with islands and strands of round cells, plasma cells, as well as some extravasated red blood cells. There was hemorrhage in some of the papillary bodies and an occasional body which was occluded by white blood cells. The elastic tissue fibers were swollen and granular.

The laboratory findings were as follows: Potassium iodide and potassium bromide patch tests gave negative results. Tuberculin tests gave positive results in 1:5000 dilution, 1 to 2+, and in 1:1000 dilution, 2+. Patch tests with penicillin ointment showed 1+ positive reaction. Negative results were obtained to therapeutic ray and oleoresin extracts from trees and grasses. Routine serological reactions for syphilis were reported negative. Complete blood cell count was taken on Oct. 20, 1952, with the following results: erythrocytes, 4,200,000; hemoglobin content, 11.3 gm. per 100 cc.; leucocytes, 9,000; neutrophiles, 43%; lymphocytes, 54%, and monocytes, 3%. Remarks—relative lymphocytosis. Urine examination showed red blood cells on two recent occasions.

Throughout the six months of treatment in this clinic, there have been periods of slight improvement with any type of therapy, with periods of exacerbation. The medications used have included petrolatum, hydrophilic base, ammoniated mercury with ichthammol (ichthyol), chlortetracycline (aureomycin), iodochlorhydroxyquin (Vioform), boric acid, neomycin ointments, and glucosulfone sodium (Promin) jelly. Cortisone was given from Oct. 8 to Oct. 27, without marked change.

DISCUSSION

DR. PAUL GROSS: On the basis of the clinical appearance of some of the lesions I would suggest another biopsy to rule out the possibility of keratosis follicularis (Darier's disease).

DR. DAVID BLOOM: I wish to suggest that we are possibly dealing with keratosis follicularis. I saw a similar case presented by Dr. Peck some years ago. The other possibility is a chronic perioral eczema.

DR. CHARLES WOLF: I wish only to offer a suggestion. Keratosis follicularis is the diagnosis I would consider least, because the eruption on the body is a pruritic papular eruption which is quite generalized. As one observer said, it looks almost like scabies. However, there is a great deal of pigmentation and the crusted lesions on the chin, which are the most conspicuous lesions to be seen, are a secondary infection. I believe I suggested to Dr. Tolmach the possibility of dermatitis herpetiformis (Duhring's disease).

DR. JESSE A. TOLMACH: I shall try vitamin A therapy in this case, but I must say that I did not and do not think that this is keratosis follicularis. The eruption on the body does not in any way resemble it.

The diagnosis of dermatitis herpetiformis is not unreasonable, and I believe that one does sometimes encounter vegetating lesions involving the mouth in this condition. To date, all tests for contact sensitivity that have been done have given negative results.

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Nov. 21, 1952

Subacute Disseminated Lupus Erythematosus. Presented by DR. M. H. SAMITZ and (by invitation) DR. A. SATANOVE and DR. B. KIRSHBAUM.

N. C., a white girl, aged 19, presented generalized erythematous papulosquamous plaques, with adherent scale. They had a predilection for the exposed areas. They were petechial hemorrhages on both the palms and the soles.

On August, 1951, during a preemployment examination, this previously healthy woman was told that she had a positive serologic test for syphilis. On repetition, the test was considered a biological false positive. In December, 1951, migratory aches and swelling of the joints of the extremities developed. A diagnosis of rheumatic fever was made, and she was given salicylates, with temporary relief of her joint pains. In March, 1952, she noticed red blotches on each cheek. She had a low-grade fever and complained of weakness and fatigue. In June, 1952, when she was 10 weeks pregnant, she was admitted to the hospital, where a diagnosis of lupus erythematosus was confirmed on bone marrow examination. All other laboratory tests at this time gave normal results.

Cortisone, 100 mg. a day for 11 days was administered, with complete remission of her lesions. She was given a maintenance dose of 75 mg. of cortisone (Cortone) daily until July 12, when the lesions had flared. On August 26 the skin lesions became intensely erythematous and spread to her trunk and extremities. Cortisone therapy was reinstituted, but, now five months pregnant, she required 150 mg. daily. On Sept. 13 she had a spontaneous abortion and after delivery had a severe flare of her lesions, despite the administration of 200 mg. of cortisone daily. She was readmitted to the Graduate Hospital on Oct. 23, at which time she presented a generalized eruption with a low-grade pyrexia and complained of weakness and fatigue.

The physical examination revealed a palpable liver and spleen, but no other abnormalities.

The serologic reactions for syphilis were negative. A complete blood cell count revealed 10 gm. hemoglobin content, 3,740,000 erythocytes, 7,400 leucocytes. The sedimentation rate was 23 mm.; the thrombocyte count, 290,000; total protein, 6.8 gm. per 100 cc. albumin, 3.85 gm., globulin, 2.95 gm.; serum chlorides, 99 mEq. (350 mg.); serum sodium, 132 mEq. (304 mg. potassium); serum potassium, 4.9 mEq. (17.9 mg. per 100 cc.). The bone marrow showed "numerous L. E. cells." A roentgenogram of the chest showed a normal picture.

On Oct. 1 quinacrine hydrochloride (Atabrine dihydrochloride), 100 mg. three times daily, produced some clearing of her lesions, but after 11 days of this medication her temperature rose to 103 F. and her leucocytes dropped to 2,100 per cubic centimeter. Quinacrine therapy was discontinued. On Oct. 12 cortisone, 50 mg. every six hours, was administered, with a dramatic drop in temperature and rapid clearing of her lesions. This dosage was decreased weekly to the present dosage of 25 mg. twice daily.

DISCUSSION

DR. M. H. SAMITZ: It is interesting that the administration of cortisone during the first trimester of pregnancy was effective in small dosage, but that during the second trimester her condition became markedly worse, and after spontaneous abortion the condition flared to a full-blown severe picture, in spite of larger doses of this medicament. This brought to mind some of the work of Venning (*Endocrinology* **39**:216, 1946) indicating that endogenous formation of cortisone is stimulated during the first trimester, while the output falls off during the second trimester.

DR. IRA L. SCHAMBERG: Within the past few years, Dr. Moore and Dr. Mohr of Johns Hopkins have been studying patients with biologic false positive reactions and they have concluded that contrary to previous impressions, in many of these patients a biologic false serologic reaction for syphilis may be of serious import; that a good percentage of these patients had collagen disease.

Sarcoidosis Treated with Quinacrine Hydrochloride (Atabrine Dihydrochloride). Presented by DR. M. H. SAMITZ and (by invitation) DR. A. SATANOVE and DR. B. KIRSHBAUM.

L. W., a Negro woman, aged 52, on Aug. 21, 1951, presented a picture of deep-seated papular lesions involving the alae nasi and the upper lip bilaterally. There were no lesions demonstrable at the time of presentation. A chalazion of the right upper eyelid was excised in 1938; she had a hemorrhoidectomy in 1941 and treatment for latent syphilis in 1942. A cyst of the neck was incised and drained in 1943. She had a hysterectomy in 1945 and a furuncle of the nose in 1947.

She has had numerous recurrences, with exacerbations of deep-seated lesions involving the alae nasi and the upper lip, from 1949 to August, 1951. A diagnosis of sarcoidosis, confirmed by biopsy, was made in August, 1951, following which a course of cortisone therapy was started, with gradual subsidence of all her lesions. The lesions recurred when cortisone was discontinued. On Feb. 6, 1952, quinacrine hydrochloride (Atabrine dihydrochloride) was administered, with gradual disappearance of her lesions.

The serologic reactions for syphilis were positive. The sedimentation rate was 23 mm. The serum calcium was 8.3 mg. per 100 cc. and total protein was 8.0 gm. per 100 cc.;

albumin, 4.18 gm. and globulin, 3.83 gm. All the other studies—complete blood cell count; urinalysis; prothrombin time determinations; sickling test; blood urea nitrogen, sugar, CO_2, Na, K, Cl, P determinations; liver studies; urinary ketosteroids, and stool examination—were within normal limits. Roentgenograms of the hands and feet showed a normal picture. Roentgenographic studies of the chest showed linear densities extending from both hilar and both lower-lung fields, representing fibrosis, possibly consistent with sarcoidosis. There was no evidence of tuberculosis, and the lung fields were otherwise negative. Repeated x-ray examinations showed no significant change.

The report on the biopsy specimen was, "granuloma, possibly sarcoid."

From February to the time of presentation, the patient was treated with quinacrine hydrochloride (Atabrine dihydrochloride) 100 mg. twice a day to three times a day, as required. The lesions disappeared, but recurred when the quinacrine therapy was temporarily suspended during October.

Sarcoidosis Involving the Mucous Membranes. Presented by DR. M. H. SAMITZ and (by invitation) DR. A. SATANOVE and DR. B. KIRSHBAUM.

J. L. W., a Negro, aged 33, in excellent physical condition, presented pinhead- to 4 mm.-sized plaques of fused flat papules localized along the central part of the upper lip and similar lesions on the medial aspects of the superior palpebrae. He also had small cystic lesions of the conjunctivae. He moved from Georgia to Philadelphia in 1945. Except for occasional flare-ups of his asthma when a "cold" develops, he has been in excellent health. In December, 1951, he noticed a "fever blister" which began in the center of his upper lip, then spread across the entire lip in one month. Two months later these little "bumps" developed on the medial aspect of both upper eyelids, with a few smaller, discrete lesions on the right cheek and beneath the alae of the nose. He had had measles and chickenpox and had been treated for latent syphilis. He had asthma from 1938 to 1945.

The medical examination revealed shotty nodes of the left axilla and epitrochlear nodes. Otherwise no abnormalities were demonstrated.

The blood cell count was within normal limits. The sedimentation rate was 10 mm. The urinalysis was within normal limits. The serologic reactions for syphilis were negative. Blood sugar was 118 mg. per 100 cc., the blood urea nitrogen, 11 mg. per 100 cc. The liver function tests gave normal results. Total protein was 7.2 gm. per 100 cc.; serum albumin, 3.78 gm. and serum globulin, 3.42 gm., serum cholesterol (total) 280 mg. per 100 cc., and serum cholesterol (free) 116 mg. A roentgenogram of the chest showed a normal picture.

The reports on biopsy specimens were as follows. March 11, 1952, lesion of the right upper eyelid—sarcoidosis (Dr. Herman Beerman); March 11, lesion of the upper lid—sarcoidosis (Dr. Herman Beerman); and April 18, lymph node from the left axilla—Boeck's sarcoid (Dr. A. De Pena).

Beginning on May 5, the patient was treated with cortisone, 80 mg. daily, which produced involution of the lesions in one month. On July 28, 1952, there was recurrence of the lesions on the lip, and cortisone therapy was discontinued. On Oct. 5 quinacrine hydrochloride (Atabrine dihydrochloride) was administered in a dosage of 2 grains (0.13 gm.) every six hours for five doses, then 1½ grains (0.09 gm.) three times daily, and this daily dosage was maintained thereafter. There was progressive diminution of the lesions of the lips and eyelids and disappearance of the conjunctival lesions. With quinacrine treatment some yellowing of the palms developed, and fluorescence of the fingernails under the Wood light appeared.

DISCUSSION
ON CASES OF SARCOIDOSIS

DR. M. H. SAMITZ: The first patient, the woman, was treated with cortisone, with almost complete regression of the lesions. We stopped the cortisone administration and the lesions returned. After quinacrine treatment was begun, the lesions regressed completely. For demonstration before the society the quinacrine treatment was discontinued, and some of the lesions recurred. The same sequence was observed in the case of the man with the lip lesions.

DR. JOHN E. GERMAN, Reading, Pa.: In February I read an abstract in *Acta dermatologica*, from *l'Algéria médicale*, Algiers (**50**:151, 1947), concerning the use of quinacrine in the treatment of sarcoid. This report was enthusiastic.

DR. M. M. CAHN: This case was presented at the last dermatological society meeting. There was almost complete regression of the nodules. That patient is still being given quinacrine (Atabrine), and after 10 months he shows no untoward effects.

Sarcoid of the Eyelids, Conjunctiva, and Uveal Tract Treated with Quinacrine Hydrochloride (Atabrine Dihydrochloride). Presented by DR. JOSEPH V. KLAUDER.

B. T., a Negro, aged 21, for 14 months has had lesions on the eyelids and for nearly as long, inflammation of the left eye that impaired vision. On both eyes, at the inner canthi, there is a lesion that partly encircles the canthi. It is firm, with a rubbery feel and yellowish color. In the outer portion of the cul-de-sac of the right eye there is a firm elongated mass that fills the cul-de-sac on the temporal side. It has an irregular surface, somewhat verrucous. Examination of the skin otherwise gave negative results.

The right eye is normal; the visual acuity is 6/6. The left eye has a complicating cataract, the remains of an old iridocyclitis. The tension is nil—phthisis bulbi. The visual acuity is light perception.

There is generalized enlargement of the lymph nodes. A roentgenogram of the chest showed no abnormalities. A roentgenogram of the hands showed coarsened trabecular pattern in the distal ends of the phalanges. The appearance was that of sarcoid.

On Oct. 20, 1952, quinacrine hydrochloride (Atabrine dihydrochloride) was prescribed, 100 mg. three times daily for two weeks, which dosage was then reduced to 100 mg. twice daily. He has been receiving this medication since that time. There has been definite improvement in the size of the lesions. This is shown in the kodachrome pictures taken at the onset of treatment and subsequently. He has gained weight and feels better.

Hapalonychia. Presented by DR. THOMAS BUTTERWORTH, Reading, Pa., for discussion of etiologic possibilities and therapeutic suggestions.

D. R. K., a white boy, aged 11, 58 in. (147.3 cm.) tall, weighing 124 lb. (56.2 kg.) (his normal weight should be approximately 88 lb. [39.9 kg.]) exhibits destruction of the distal parts of all the fingernails, with the exception of the right index finger. The nails of the first two toes of both feet are similarly destroyed. The proximal portions that remain are smooth and pink and soft. There have been no striking changes in the nail folds. The destruction was gradual, beginning in the middle of the summer of 1951. The patient stated that pus has been expressed from the nail folds, although the presenter has never seen this in nine months of observation. There was nothing abnormal in the general physical examination, other than the fact that the penis is considerably smaller than normal. The testes, however, are normal in size and consistency. Complete measurements were made, and the only abnormal findings were in the trochanteric circumference.

Culture revealed no mycotic growth. The basal metabolic rate was —8. The blood sugar was 67 mg. per 100 cc.

Superficial x-ray therapy, calcium lactate, and mixed vitamins have failed to change the clinical picture.

DISCUSSION

DR. FRED D. WEIDMAN: He looks "pituitary" to me. He has a rather low hairline and there is a remark on the protocol about the external genitalia. I think that it would be a good idea to check for further evidence of pituitary abnormality.

DR. THOMAS BUTTERWORTH, Reading, Pa.: I found mention of this condition in Pardo-Castello's text, in which he states that he has seen three cases. The condition is associated with leprosy, chronic arthritis, myxedema, acroasphyxia, peripheral neuritis, and hemiplegia. The patient has been studied by an endocrinologist, who performed all the

measurements and went through all the tests that endocrinologists perform, and he was not able to give us a definite conclusion. I may try a little thyroid therapy to see if it helps him.

DR. MEYER L. NIEDELMAN: Someone reported some years ago the use of bismuth by mouth for soft nails. It might be worth trying.

DR. FRED D. WEIDMAN: Do you think it a trophic disorder?

DR. THOMAS BUTTERWORTH, Reading, Pa.: Pardo-Castello refers to Dr. Klauder's work on the sulfur content of the nail and suggests hydrolyzed wool. Of course, Dr. Klauder did that work some 20 or 25 years ago, and only recently a commercial company has offered hydrolyzed wool as a commercial product.

Pyoderma Gangrenosum. Presented by DR. M. H. SAMITZ and (by invitation) by DR. A. SATANOVE and DR. B. KIRSHBAUM.

Dermoepidermal Nevi with Beginning Malignant Melanoma Changes. Presented by DR. M. H. SAMITZ.

Lymphocytoma Cutis. Presented by DR. M. H. SAMITZ.

Recurrent Squamous-Cell Carcinoma of the Tongue. Presented by DR. M. H. SAMITZ.

Chronic Ulcer of the Leg. Presented by DR. SAMITZ and (by invitation) by DR. A. SATANOVE and DR. B. KIRSHBAUM for diagnosis and treatment.

Bilateral Ulcers of the Legs Associated with Sickle-Cell Anemia. Presented by DR. M. H. SAMITZ and (by invitation) by DR. SATANOVE and DR. B. KIRSHBAUM.

Seborrheic Diathesis with Bacterial Overlay (Proteus Vulgaris). Presented by DR. M. H. SAMITZ and (by invitation) by DR. A. SATANOVE and DR. B. KIRSHBAUM.

Lupus Vulgaris. Presented by DR. M. H. SAMITZ and (by invitation) by DR. A. SATANOVE and DR. B. KIRSHBAUM.

Rhinophyma—Plastic Repair with Monopolar Cutting Current. Presented by Dr. MEYER L. NIEDELMAN.

Case for Diagnosis. Presented by DR. THOMAS BUTTERWORTH, Reading, Pa., and DR. JOHN E. GERMAN.

Dermatitis Herpetiformis Treated with Chloretetracycline (Aureomycin). Presented by DR. M. H. SAMITZ and (by invitation) by DR. A. SATANOVE and DR. B. KIRSHBAUM.

Fred D. Weidman, M.D., *Chairman*

Bertram Shaffer, M.D., *Secretary*

Feb. 20, 1953

Multiple Acanthoma (Tumor-Like Keratosis of Poth). Presented by CAPTAIN W. M. NEW (MC), U.S.N., and COMMANDER S. H. HORTON (MC), U.S.N. (by invitation).

H. F. Q., a white man, aged 54, fairly well developed, well-nourished, in no acute distress, presented two types of lesions: (1) heaped-up firm nodular lesions with a thick adherent kertatinous summit, and (2) superficial bluish atrophic plaques on the face, forehead, ears, and arms. There were also a few keratotic lesions on the "V" of the neck, the nape, and the extensor surfaces of the forearms. The hypertrophic lesions predominated. All were a violaceous color and very dry.

Four years ago a reddish spot developed on the left side of his forehead. Later, new lesions appeared, most of which were raised and crusted, on the forehead, the scalp, the neck, about the ears, and on the extremities. Some have regressed, leaving a light scar. These lesions are asymptomatic. The condition is much worse in summer, and after a day at the beach he sometimes finds new lesions. He is a carpenter and house painter. He came to the hospital on account of pains in the stomach aggravated by fried foods and corn. He has nausea but seldom vomits.

Except for the abdominal complaints, the internal medical examination gave essentially negative results.

Examination of the feces disclosed no blood or ova; the sulfobromphthalein (Bromsulphalein) sodium test showed 20% retention; cephalin flocculation, 4+; a blood cell count showed 15 gm. hemoglobin content, 7,600 leucocytes; the Kahn serologic reaction for syphilis was negative; total protein was 6.4 gm. per 100 cc. of blood; albumin, 3.9 gm. and globulin, 2.5 gm. Urinalyses gave negative results. There was no fluorescence under the Wood light.

The report on the biopsy specimen by Dr. Fred D. Weidman was, "acanthoma (tumor-like keratosis of Poth)."

DISCUSSION

DR. FRED D. WEIDMAN: The lesions on the forearms are letter-perfect for those described by Dr. Poth and are the most extensive on record. I suspect that Dr. New will write up the case from that standpoint. It is a light-sensitization dermatosis reflecting its maximum expressions in the form of these tumor-like keratoses or acanthomas.

DR. IRA L. SCHAMBERG: Do these tumors remain benign?

DR. FRED D. WEIDMAN: Yes, and they may disappear spontaneously.

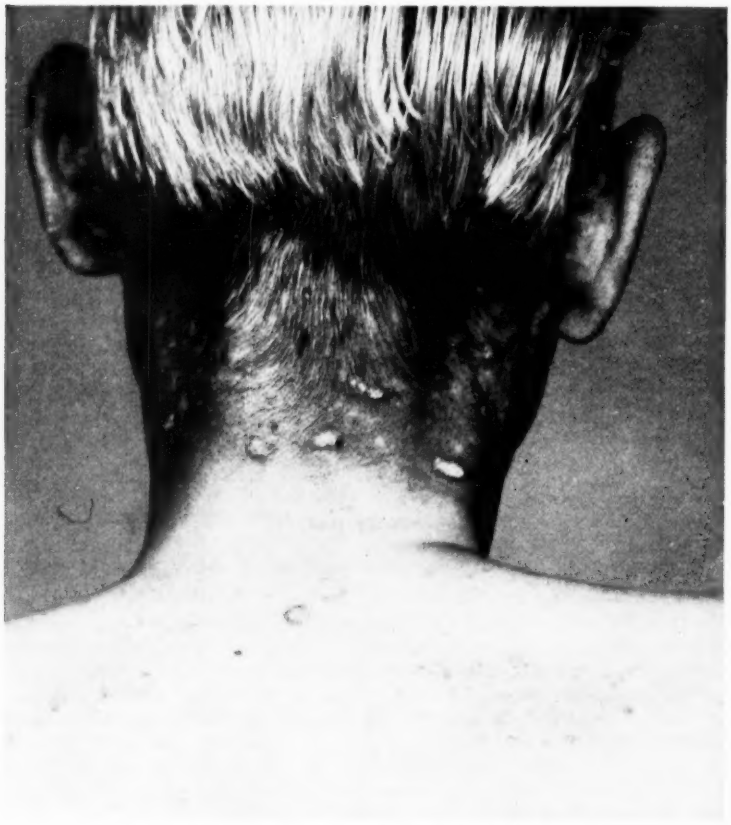


Fig. 1.—Acanthoma (tumor-like keratosis of Poth).

DR BERTRAM SHAFFER: Are there any systemic manifestations in this disease such as we find in lupus erythematosus, and on what basis is the statement made that this is a light-sensitization dermatosis? Does the eruption improve in the winter and flare in the summer, or is the presumed etiology based solely on the distribution?

DR. FRED D. WEIDMAN: Largely on the distribution, and there are no systemic symptoms. Poth's cases were confined to the hands, but in the present patient the lesions are distributed additionally on other exposed parts—a light-sensitization distribution comparable to that of lupus erythematosus.

CAPTAIN W. M. NEW (MC), U.S.N.: The scarring on his scalp I think is the result of the disease.

DR. FRED D. WEIDMAN: They are lesions that have regressed.

DR. HERMAN BEERMAN: I thought that these lesions looked like hypertrophic lichen planus.

COMMANDER S. H. HORTON (MC), U.S.N. (by invitation): In 1939 Duncan Poth reported a case in which the patient was severely sunburned, and subsequently seven translucent hard keratinous-topped lesions developed on the dorsa of the hands. Biopsy sections were sent to Dr. Montgomery, who made a diagnosis of verruca vulgaris, to Dr. Wile, who made

Fig. 2.—Acanthoma (tumor-like keratosis of Poth).

a diagnosis of hyperkeratosis; to Dr. Todd and Dr. Belote, who made a diagnosis of carcinoma, and to Dr. Weidman, who made the diagnosis of tumor-like keratosis. All these lesions underwent spontaneous involution. In 1946, Ayres presented a case with a diagnosis of squamous-cell epithelioma, self-healing type. Dr. Montgomery, in discussing the case, said he did not believe that squamous-cell carcinoma ever underwent spontaneous involution and that he believed the condition was lupus erythematosus. In September, 1952, Fliegleman reported a case in which the patient had been exposed to the sun; lesions

developed on the dorsa of the hands and looked very much like the case tonight, and they underwent spontaneous involution. This patient came to the hospital on account of hepatic disease. He is asymptomatic.

DR. FRED D. WEIDMAN: The message from this presentation is that there is one more condition which may enter into the differential diagnosis of lupus erythematosus; at least, if one gives very much weight to the anatomic distribution and to the atrophic macules. Of course, the full-fledged individual lesions are impossible for that.

Sarcoidosis? Lupus Vulgaris? Benefited by Isoniazid. Presented by DR. CARROLL F. BURGOON.

Urticaria Papulosa (Lichen Urticatus). Presented by DR. H. H. PERLMAN and (by invitation) DR. J. DOUBRESSE.

Insect-Bite Reaction? Spontaneous Keloid? Presented by DR. CARROLL F. BURGOON, for diagnostic and therapeutic suggestions.

Nevus Epitheliomatocylindromatosus. Presented by DR. LESLIE NICHOLAS.

Neurodermatitis; Hypertrophic Lichen Planus. Presented by DR. DOROTHY R. LYNN.

Papulonecrotic Tuberculid? Presented by DR. JOHN M. SIEGEL, Allentown, Pa.

Case for Diagnosis. Presented by DR. DOROTHY R. LYNN.

Case for Diagnosis. Epidermolysis Bullosa? Presented by CAPTAIN W. M. NEW (MC) U.S.N.

Psoriasis of Penis? Presented by DR. JOHN P. SCULLY, Reading, Pa.

Cutaneous Tuberculosis; Lupus Vulgaris? Rosacea-like Tuberculid; Lupus Miliaris Disseminata Faciei? Presented by DR. BERTRAM SHAFFER and (by invitation) DR. I. HARDIN and DR. M. M. CAHN.

Histiocytoma Cutis in Infant 6 Months of Age. Presented by DR. JOHN P. SCULLY, Reading, Pa.

Urticaria Pigmentosa. Presented by DR. CARROLL F. BURGOON.

Bullous Lupus Erythematosus; Pemphigus Erythematosus (Senear-Usher Syndrome); Dermatitis Herpetiformis? Presented by DR. J. M. SCHILDKRAUT, Trenton, Pa.

Acute Disseminate Lupus Erythematosus. Presented by DR. CARROLL F. BURGOON: (Presented because of apparent remission produced by a combination of quinacrine hydrochloride [Atabrine dihydrochloride] and corticotropin [ACTH].)

Case for Diagnosis. Presented by DR. LOUIS JAFFE.

Lupus Vulgaris. Presented by DR. LOUIS JAFFE and (by invitation) DR. RUDOLPH K. GLOCKER and DR. JOHN MARON.

News and Comment

ANNOUNCEMENTS

American Academy of Dermatology and Syphilology.—The next annual meeting of the American Academy of Dermatology and Syphilology will be held at the Palmer House, Chicago, Dec. 5-10, 1953.

Continuation Course in Dermatology.—Dermatology will be the subject of a continuation course for physicians which will be presented by the University of Minnesota at the Center for Continuation Study next Nov. 19 to 21. Intended primarily for physicians engaged in general practice, the course will stress the recognition and management of the common skin disorders. The program will be presented under the direction of Dr. H. E. Michelson, Professor of Medicine and Director of Dermatology, and the remainder of the faculty will be drawn from the University of Minnesota Medical School and the Mayo Foundation.

Lodging and meal accommodations are available at the Center for Continuation Study.

Establishment of a Beryllium Case Registry.—The Massachusetts General Hospital plans to develop a Beryllium Case Registry with funds supplied by the Atomic Energy Commission. Its purpose is to enable a study of the epidemiology of this disease, an evaluation of the beryllium hazard of incriminated operations, and dissemination of knowledge of the clinical course of beryllium poisoning, especially in relationship to its medical management.

Physicians, roentgenologists, and pathologists with knowledge of beryllium poisoning are encouraged to participate in this study. Facilities and funds are available for handling case records, x-rays, and tissues which are submitted.

Data will be sent to participating physicians from time to time summarizing facts that have been established.

Cases submitted will remain anonymous. They should be sent to Dr. Harriet L. Hardy, Associate Physician, Occupational Medical Clinic, Massachusetts General Hospital, Boston 14.

INTERNATIONAL CONFERENCE ON GROUP PSYCHOTHERAPY

The International Committee on Group Psychotherapy is preparing a meeting on group psychotherapy in Toronto, Canada, in connection with the Fifth International Congress on Mental Health, to be held August, 1954. The conference will promote the exchange of information and intensify personal contact between group therapists and group workers throughout the world.

An all-day series of meetings is planned for Thursday, Aug. 12, in Toronto. The morning meeting will discuss the use of the group in mental health and in psychotherapy. Current practices in group psychotherapy with adults and with children and parents will be the topic for afternoon and evening meetings.

Representatives from 17 nations are sponsoring the meeting. They will present papers on various recent developments in the use of group psychotherapy, e. g., with alcoholics, with delinquents, with the aged, etc. The use of the group in education, in recreation, in industry, and in government will be discussed. In addition, plans are being made for a dinner meeting and get-together of this international group.

The sponsoring committee is as follows: E. E. Krapf (Argentina); D. Ewen Cameron, Miguel Prados, W. Donald Ross, Aldwyn Stokes (Canada); Carlos Nassar (Chile); Paul J. Reiter (Denmark); T. P. Rees (England); G. Heuyer, Serge Lebovici (France); H. C. Rumke (Holland); C. Frankenstein, L. Miller (Israel); A. Godin (Italy); Masao Otsu

(Japan); Luis Feder (Mexico); S. Bankole-Wright (Nigeria); Nic Waal (Norway); C. Alberto Seguin (Peru); C. H. de C. Murray (South Africa); Gösta Turner Harding (Sweden); Lewis H. Loeser, Joseph H. Pratt, Fritz Redl, S. R. Salvson, Edward A. Strecker (United States); chairman: Wilfred C. Hulse, M.D.

For full details write to Dr. Wilfred C. Hulse, chairman, International Committee on Group Psychotherapy (sponsored by the American Group Psychotherapy Association, Inc.), 110 W. 96 St., New York 25.

CORRECTION

In the article by Dr. Lee J. Alexander, "Desensitization of the Penicillin-Sensitive Patient," published in the September, 1953, issue of the ARCHIVES, the third sentence on page 327 should read: "Because of her extreme sensitivity it was necessary to begin the desensitizing procedure with an initial dose of 2 units of aqueous penicillin."

The officers of the Cleveland Dermatological Society, as well as of the Central States Dermatological Association, for the year 1953-1954 are:

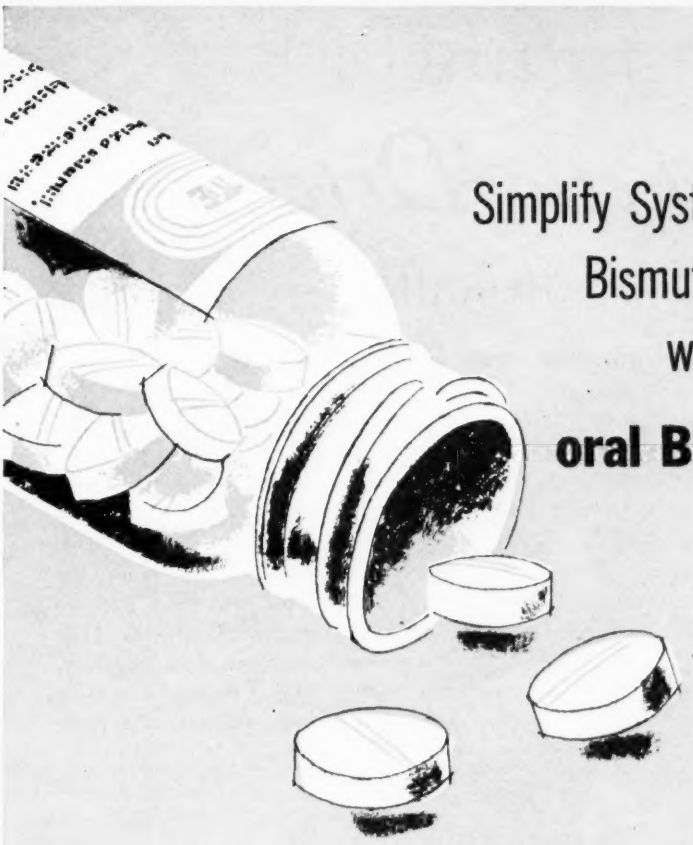
Herbert H. Johnson Jr., President, 10515 Carnegie Ave. (6).

Benjamin P. Persky, Secretary, 2060 East 9th St. (15).

In the article by Ruiter appearing in the July, 1953, issue of the ARCHIVES (Ruiter, M.: Angiokeratoma Corporis Diffusum, **68**:21, 1953), the first two sentences of the fourth paragraph on page 26 should read as follows:

"In my opinion, the essential pathological process in angiokeratoma diffusum consists in dilatation of preexistent vessels, in which the capillaries of the stratum papillare are particularly affected. Like Scriba, I believe that in respect to the origin of the angiectatic lesions in the cases discussed in this article a decrease of vascular tonus, caused by the changes observed in the muscular coat of the blood vessels, has been of importance. . . ."

In the Directory of Dermatologic Societies, published in the July, 1953, issue, an error appears in the listing of officers of the Detroit Dermatological Society. Dr. Coleman Mopper, 302 Holbrook Building, Detroit 12, is Secretary-Treasurer of the Society.



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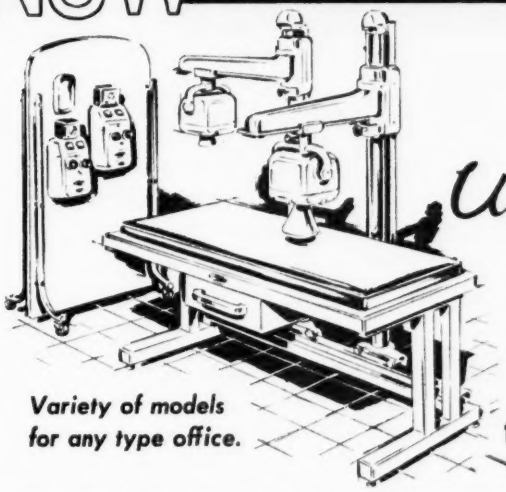

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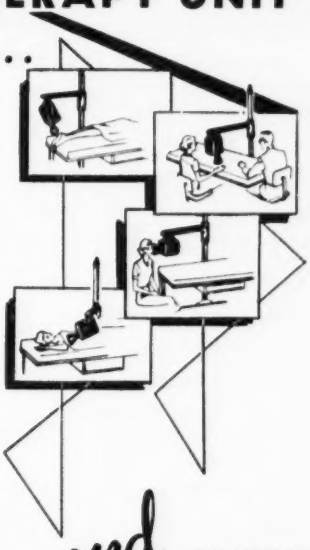

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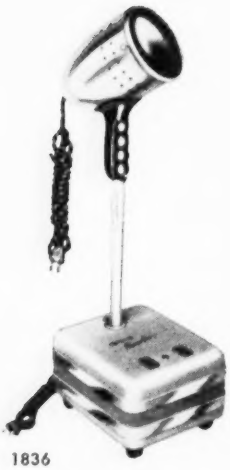

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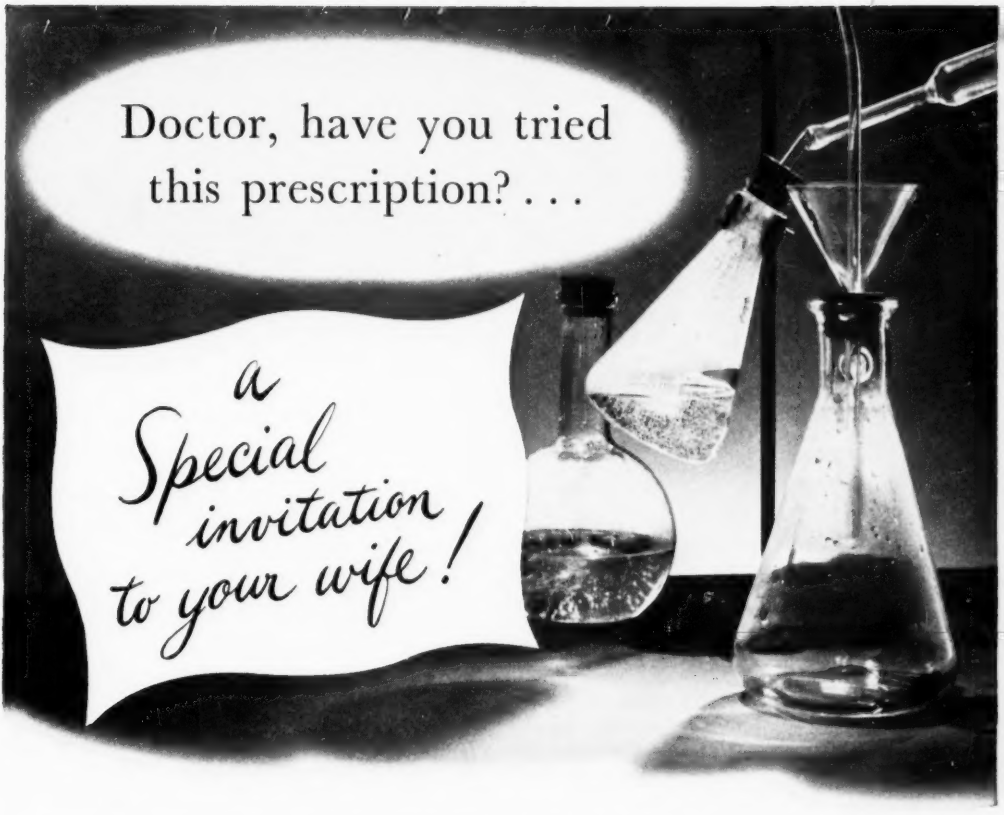

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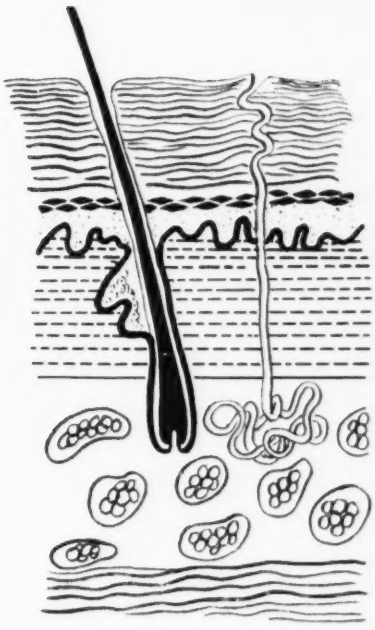

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